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Microwave/Radiofrequency (MW/RF) Radiation Exposure and Cancer Risk: Meta-Analysis of Accumulated Empirical Evidence

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Abstract

Background: Scientific debate regarding the health effects of Microwave/Radiofrequency (MW/RF) radiation has continued for decades, but has risen sharply in recent years due to an explosion in wireless technology. Several studies of the health effects of MW/RF radiation were published in recent years, but their results have not been analyzed to date using meta-analysis tools.

Study goal: To analyze the accumulated body of scientific evidence regarding cancer risk associated with MW/RF radiation exposure in environmental and occupational studies.

Methods: 57 studies, published over 30 years, between 1982 and 2012, and relating to the association between MW/RF radiation exposure and cancer risks were analyzed using meta-analysis tools of the WinPepi© software.

Results: The meta analysis indicates an elevated risk of morbidity and mortality from several types of cancer associated with exposure to MW/RF: lymphoma morbidity Overall Ratio (OR) = 1.55 (95% CI 1.22, 1.97); childhood leukemia morbidity OR =1.35 (95% CI 1.17, 1.56); adult leukemia morbidity OR = 1.24 (95% CI 1.12, 1.37); and mortality OR = 1.29 (95% CI 1.13, 1.47); melanoma morbidity OR = 1.47 (95% CI 1.24, 1.74); breast cancer morbidity OR = 1.23 (95% CI 1.10, 1.39); brain and central nervous system (CNS) cancer morbidity OR = 1.44 (95% CI 1.18, 1.74); all cancer sites morbidity in adults OR = 1.11 (95% CI 1.06, 1.16) and all cancer sites in children and adults OR = 1.07 (95% CI 1.03, 1.11).

Concurrently, no statistically significant association was found for brain and CNS tumors morbidity in children Overall Ratio (OR) = 1.11 (95% CI 0.94, 1.32); lymphoma and multiple myeloma mortality OR = 1.17 (95% CI 0.96, 1.42); all cancer sites mortality OR= 0.92 (95% CI 0.88, 0.97) and mortality from brain and CNS tumors, OR = 1.18 (95% CI 0.94, 1.48). In addition, studies recorded differences in cancer risk across different age groups, and the effect of promotion (acceleration) was also recorded, expressed by a shorter latency period in the exposed vs. non-exposed.

Conclusions: Accumulated empirical evidence points to an increased risk of lymphoma, leukemia, melanoma, breast and brain/CNS cancers associated with exposure to MW/RF radiation. The existing safety standards may not be sufficient to protect the public and workers from exposure to MW/RF radiation and should be revised to account for a potentially long term effect of exposure to MW/RF radiation. Children exposures to MW/RF radiation should be restricted.

Keywords

Microwave and radiofrequency (MW/RF) radiation, Cancer, Occupational exposure, Environmental exposure, Meta-analysis.

Introduction

The World Health Organization's (WHO's) International Agency for Cancer Research (IARC) classified both Extremely Low Frequency (ELF) Magnetic Fields and Radio Frequency Radiation (RFR) in Group 2B Human Carcinogen [1-3].

Scientific debate over the potential risk attributed to MW/RF radiation has increased dramatically in recent years due to increased concerns as wireless technologies saturate the home and workplace.

Deshmuckh et al. [4] found DNA strand breaks in rat brains after being exposed to low intensity microwave radiation at the lower, middle and upper frequencies used in mobile telecommunication. The researchers concluded that although microwave energy is not sufficient to break the chemical bonds in DNA directly, genotoxic effects may be mediated by indirect mechanisms, such as generation of oxygen free radicals or a disturbance in DNA-repair processes (*ibid*).

In another study Burlaka et al. [5] on quail embryos, it was found that exposing cells to extremely low intensity RFR (900 MHz for 158-360 hours discontinuously), before and during the initial stages of development, led to a significant overproduction of free radicals. In particular, the levels of 8-OHdG (a common biomarker of oxidative damage to the DNA) in the cells was found to increase

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2-3 fold compared to the controls. This study found that especially low intensity MW/RF radiation (0.25 μW/cm^2; SAR = 3 μW/kg) led to oxidative DNA damage. Based on the evidence, the authors of the study concluded that the oxidative changes may develop in pathology leading to oncogenic transformation of cells.

Yakymenko et al. [6] reviewed epidemiological evidence from radars and mobile communication systems studies. The researchers found that under certain conditions, exposure to long term low intensity MW/RF radiation led to initiation and promotion of cancer. Yakymenko concluded that recent data strongly indicate the need for concern and transparency of the current safety limits for non-ionizing radiation using recently obtained knowledge. Summarizing laboratory evidence on oxidative damage to cells, Yakymenko et al. [7] reviewed 80 peer reviewed publications, of which 76 (92.5%) reported the detection of significant oxidative stress from MW/RF radiation. The authors noted that significantly increased levels of reactive oxygen species (ROS) in living cells caused by low intensity MW/RF radiation exposure, may promote mutagenic effects through oxidative damage in the DNA. They also noted, that overproduction of ROS in living cells under low intensity exposure could cause a broad spectrum of health disorders and diseases, including cancer in humans. Within one year, the number of studies they reviewed increased to 100, of them 93 confirmed that MW/RF radiation induces oxidative effects in biological systems. Molecular effects induced by low-intensity in living cells included significant activation of key pathways generating ROS, activation of peroxidation, oxidative damage of DNA and changes in the activity of antioxidant enzymes. The authors concluded that oxidative stress should be recognized as one of the primary mechanisms of the biological activity of this kind of radiation [8].

Levitt and Lai [9] found that broadcast exposures had been found unsafe even at regulated thresholds, noting significant increases for all cancers in both men and women living near broadcast towers and leukemia clusters in children and adults. They found also, that 56 of 56 studies reported biological effects at very low intensities of MW/RF radiation, including DNA damage in human glial and leukemia cells, effect on the DNA repair mechanism and indication of an increase in glioma cells division.

Regarding epidemiological evidence, reviews of occupational and environmental studies of cancer-related effects from exposure to MW/RF radiation, varied in conclusions. Elwood [10], Ahlbom et al. [11] and Breckenkamp et al. [12] found inconsistent epidemiological evidence.

Carpenter [13,14] stated in his reviews, that excessive exposure to MW/RF radiation increased risk of cancer, with the strongest evidence coming from studies on cell phone users, whereas results were not consistent across all studies that reported elevations in both leukemia and brain tumors among individuals with occupational exposure to MW/RF radiation. The author pointed to more recent reports that found elevated rates of leukemia among children who lived near AM radio transmitter sites.

Kundi and Hutter [15] reviewed effects of base stations, and found that only two studies had been published on cancer [16,17]. Both of them found increased risk, but had no individual data and therefore were considered to provide limited evidence, and no firm conclusions could be drawn.

Khurana et al. [18] included the same two studies in the review, concluding that altogether increased prevalence of adverse neurobehavioral symptoms or cancer in populations living at distances of < 500 meters from base stations prevalence of adverse neurobehavioral symptoms were found in 80% of the available studies. The authors recognized methodological weaknesses, especially since exposure to MW/RF radiation was not always measured. However, they noted that none of the studies they reviewed, revealing adverse health effects from base stations, reported exposures to MW/RF radiation above accepted international guidelines. The researchers concluded, that if such findings continue to be reproduced, current exposure standards are inadequate in protecting human populations.

To the best of our knowledge, the present study is the first of its kind, which aims to quantify the evidence of association between MW/RF radiation and cancer, in both occupational and environmental settings, using meta-analysis tools.

Study Methods

Association ratios

We considered all types of association ratios reported in the literature, including Odds Ratio (OR) reported in 19 studies; Relative Risk or Rate Ratio (RR) reported in 11 studies, Standardized Incidence Ratio (SIR) used in 4 studies, Proportional Incidence Ratio (PIR) used in 1 study, Proportional Mortality Ratio (PMR) reported in 5 studies, Proportional Registration Ratio (PRR) reported in 1 study, Standardized Mortality/Morbidity Ratio (SMR; O/E = observed/expected) reported in 10 studies, Mortality Rate Ratio (MRR) reported in 1 study, and crude death rate per 1000 reported in 1 study. The ratio of the 'observed to expected' is called SMR (standardized mortality ratio), SIR (standardized incidence ratio) or when death is the outcome, the standardized mortality ratio, SMR [19]. Proportional Mortality Ratio (PMR) gives results similar to SMR (personal communication with Dr. Sam Milham; Decoufle 1980) [20], while for a disease like cancer, the RR is approximately equal to the OR [21]. The calculation that is used in WinPepi© is valid in a meta-analysis where different units of measurements are used in different studies (WinPepi© manual).

Data sources

We analyzed the peer reviewed papers published between 1982 and 2012 dealing with the association between MW/RF radiation and cancer in both environmental and occupational settings. The studies were found using the Medline and Google scholar search engines or based on previous knowledge. Altogether we reviewed 57 papers that included different end points (morbidity, mortality and 1 survival study) in different ages (children and adults).

Out of the 57 studies collected, 4 studies were excluded because they did not contain epidemiologic analysis [22,23] reported a very high result that masked results of other studies in disproportion [there was one underlying cause of death due to leukemia compared with 0.2 expected (standard mortality ratio [SMR] = 437, 95% confidence interval [CI] = 11-2433), and two multiple listed causes of death due to leukemia compared with 0.3 expected (SMR = 775, 95% CI = 94-2801) [24]] or used a case series method with no epidemiological ratios and/or probability values [25]. Out of the remaining 53 studies, described in Table 1, we discarded for use in the meta-analysis 6 studies without information on confidence intervals or indications on how to extract them [26-31] and one study in which the CI was reported to be higher than the actual measure of association [RR = 4.15 95% CI 40.1, 217.2 [17]]. From the total collected, we used 46 studies (81%) for the meta-analysis.

Use of WinPepi© program

The analysis was performed by the meta-analysis module of the WinPepi program COMPARE2 [32] using a fixed-effect model. In the fixed-effect model, it is assumed that the individual studies provide estimates of the same results [33].

The WinPepi computers programs for epidemiologists were designed as learning or teaching aids for use in practice and research in the health field. WinPepi is the Windows version of the DOS-based PEPI (an acronym for Programs for *EPI*demiologists) package, which grew from a set of programs for programmable pocket calculations published in 1983 [34].

Results

The results are presented in Table 2, Figure 1, Figure 2, Figure 3 and Figure 4. Overall, MW/RF radiation was recorded in studies to be associated with a statistically significant increased risk of morbidity of

Table 1: General description of studies

Study	Study design, types of cancer outcome and type of exposure	Confounders	No. of Subjects/population	Source of data
Baumgardt-Elms [56]	Case control, morbidity, testicular, occupational	Matched by age and region	1066	Clinical and pathology departments in 5 regions in Germany,Interviews
Berg [57]	Case control brain tumors, occupational	Age, gender (matched), socioeconomic status, urban vs. rural area, ionizing radiation, smoking, cell phone, demographic characteristics, transmitters and ham radio, smoking and medical histories, occupational exposure to EMF	2241	Interviews, questionnaire. Four neurological clinics in Germany, population registries
Calle [58] Letter	Proportional mortality ratio, leukemia, occupational	Adjusted for age and year of death	6 radio and telegraph operators (observed)	Wisconsin Department of Health and Social Services
Cantor [46]	Case control, mortality, breast cancer, occupational	Adjusted for age and socio economic status	108,989 white women, 16,033 black women	National Cancer Institute, the National Institute for Occupational Safety and Health (NIOSH) and the National Center for Health Statistics
Chung –Yi [41]	Ecological morbidity, all site cancers, leukemia and brain tumors, environmental	Age, gender, ELF, calendar year of diagnosis, urbanization level of township	2606 including 939 leukemia and 394 brain cancer	National health Insurance Research Database, Taiwan National Communication Council
Coleman [59] Letter	Proportional registration ratio(PRR), leukemia, occupational	5-year age group, adjusted for age	8 cases of telegraph/radio operators	South-East England, South Thames Cancer Registry
Cooper [60] Letter	Ecological, morbidity, leukemia, environmental	Stratified by 5-year age bands, gender and socioeconomic status	20 leukemia cases	West Midlands Cancer Intelligence Unit database (Birmingham, England)
Degrave [35]	Cohort mortality, all types, occupational	Age	7349	Military, Belgian National Registry, Belgian National Cancer Registry
Davis [61]	Cohort, morbidity, testicular, occupational	Testes disease or trauma, family history of testicular cancer, occupational exposure to pesticides and herbicides	340 police officers	Interviews, SEER 1981 registry rates. Pathology slides
Demers [62]	Case control, morbidity, breast cancer, occupational	Age, work history, a broad range of risk factors (not detailed), education	527 total, 12 communication and broadcasting exposure, males	Cancer registries and National Cancer Institute, Interviews
Dode [31]	Ecological mortality, all site cancers, environmental	Age, gender	7191	Health Department of the city Belo Horizonte in Brazil, Brazilian Telecommunication Agency, Brazilian Institute of Geography and Statistics
Dolk [63]	Ecological, morbidity, all types, environmental	Age, socioeconomic class	408,000 males and females	National Statistics office UK, cancer registry, British Broadcasting Corporation. Population and cases were located via postcode of residence
Dolk [64]	Ecological, morbidity, leukemia, melanoma, bladder, childhood leukemia and brain, environmental	Age, socioeconomic_status	3.39 million males and females	National Statistics office UK, cancer registry, British Broadcasting Corporation. Population and cases were located via postcode of residence
Eger [16]	Case control morbidity, all types, environmental	Age, gender	1000	Medical records
Elliot [65]	Case control, Brain and CNS, leukemia, non Hodgkin's and all cancers, environmental	Gender, date of birth, education, deprivation measure, population density, population mixing	6985 children	All the registered cases of cancer in children aged 0-4 in Great Britain in 1999-2001. Four national mobile phone operators provided data
Finkelstein [66]	Cohort morbidity all types, occupational	Age, calendar year	12 leukemia cases, 41 melanoma cases	Ontario cancer registry, 83 Ontario police departments
Goldsmith [47] analysis of Lilienfeld 1978	Cohort mortality, all site cancers, leukemia, breast, brain, occupational	Not stated		Lilienfeld 1978
Goldsmith [36] analysis of Robinette 1980	Cohort mortality all types, occupational	Year of birth	40,000 Korean war Naval personnel	Navy and Veterans Administration records
Goldsmith [47] analysis of Anderson 1986	Ecological morbidity, All site cancers and leukemia, environmental	Age	1143 cases of all site cancers in males and females 26 leukemia cases in males and females	Honolulu Cancer Registry, EPA radiation measurements
Grayson [67]	Nested case control, morbidity brain tumors, occupational	Age, race, military rank as a surrogate for socioeconomic status. Cases and controlled were matched	1150 males	US Air Force personnel records

Groves [68]	Cohort mortality, all types, occupational	Age	40,581 total 20,021 high exposure, males	Department of Veterans Affairs. Job classification from US Navy Veteran cohort, industrial hygienists
Ha [45]	Ecological, morbidity, all site cancers, breast, leukemia, lymphoma, brain cancer, environmental	Age	3152 -126,523 people per area	Clinical and pathology departments in 5 regions in Germany, Interviews
Ha [42]	Case control morbidity, leukemia and brain tumors, environmental	Matched on age, gender and year of diagnosis. Residential location, population density and socioeconomic status, industrialized environmental pollution	5966 children (up to 15 years old)	South Korean Medical Insurance Data system, National Cancer Registry
Hardell [69]	Case control, testicular, occupational	Selection of the closest subjects in birth registration number (born in the same year)	462 total 5 radar workers	Swedish Cancer Registry
Hayes [70]	Case control, morbidity, testicular, occupational	Age, radioisotopes, radioactive materials or nuclear materials, pesticides, polycyclic aromatic hydrocarbons	530 males	Three collaborating medical institutions in Washington DC area, two of the study hospitals were military hospitals
Hocking [71]	Ecological, morbidity and mortality, children and adults, leukemia and brain tumors, environmental	Age, gender, calendar period, area	585,000 males and females	New South Wales Cancer Registry (Australia), Commonwealth Department of Communication and Arts
Hocking [39]	Survival ecological, leukemia, environmental	Age, gender and year of diagnosis	160 children	New South Wales (Australia) cancer registry
Holly [72]	Case control, morbidity Uveal melanoma, occupational	Demographic characteristics, occupational history, and exposure to chemicals. Excluded home microwave ovens	668 males	Ocular Oncology Unity at the University of California San Francisco, interviews
Karipidis [73]	Case control, morbidity non Hodgkin's lymphoma, occupational	Matched on age, gender and area of residence. Occupational exposure, risk factors of NHL, ionizing radiation, chemicals	1388 males and females	New South Wales Central Cancer Registry, Australia. New South Wales and Austrian Capital Territory electoral polls
Karipidis [74]	Case control, Morbidity Glioma, occupational	Age, gender, postcode of residence. Occupational exposure, education. Job exposure matrix included exposures to ELF, RF, UV and ionizing radiation	838	14 Melbourne hospitals, Victoria Cancer Registy, major population centers in the state of Victoria, Australia. Questionnaires and interviews
Kliukiene [75]	Nested case control within a cohort, morbidity breast cancer, occupational	Job histories, Match on year of birth, exposures	495 within a cohort of 2619	National cancer registry of Norway
Lagorio [30]	Cohort mortality, all site cancers, leukemia, brain, Digestive, liver, lung, breast, occupational	Age, gender, calendar period – specific regional mortality rates to the person years at risk	481 females	Registry Office of the municipalities
Maskarinec [76]	Case control morbidity, leukemia, environmental	Age, gender, medical history, exposure to metals, smoking in the home, X rays, proximity to oil drums, parents occupational history and exposure to metals, chemicals. Case and controls were matched on gender and age	60 cases and controls, children	Hawaii Tumor Registry, Interviews
Mcdowall [27] Letter	Proportional mortality ratio (PMR), leukemia, occupational	----	6 telegraph radio operators (no. of cases)	Office of population censuses and surveys, England and Wales electrical occupations
McKenzie [77]	Ecological, leukemia morbidity, environmental	Age and socioeconomic status	216 children	New South Wales Central Cancer Registry
Merzenich [78]	Case control morbidity, leukemia, environmental	Age, gender and transmitter area (matching), population density	7807	German childhood cancer registry (1984- 2003)
Michelozzi [79]	Ecological, mortality, morbidity, childhood and adult leukemia, environmental	Age, gender, socioeconomic class	49,656 adults and children	Lazio Region Geographic information mortality system, Italian Cancer Registries, main hospitals in Rome, Residence data: local population register, and census tract
Milham [29] Letter	Proportionate mortality ratio (PMR), leukemia, occupational	Standardized by age and year of death	5 radio and telegraph operators, 5 TV and radio repairman, no. of observed	All deaths of Washington State. Washington State department of Social and Health Services
Milham [80]	Proportionate Mortality Ratio (PMR), leukemia, lymphoma, lung, brain, pancreas, occupational	Age, year of death	486,000 males total	Records of male deaths filed in Washington State
Milham [81] Letter	Proportionate mortality ratio (PMR), leukemia occupational	Age	1691 male deaths. Of them 24 with leukemia	Washington State and California, radio operators monthly magazine that lists deaths on monthly basis

Milham [82]	Cohort mortality, all types, occupational	Age	67,829 amateur radio operators	US Federal Communications Commission Amateur Radio Station and/or Operator License file from the National Technical Information Services
Milham [26]	Cohort, mortality, Hematologic, lymphatic and brain cancer, occupational	Age	67,829 amateur radio operators	US Federal Communications Commission Amateur Radio Station and/or Operator License file from the National Technical Information Services
Morgan [83]	Cohort, mortality, brain, lymphatic/ hematopoietic, Hodgkin's, melanoma, respiratory system, stomach, breast, occupational	Age, gender, race	195,775 total 24,621 exposed	National Death Index, Social Security Administration, archived personnel files
Pearce [84]	Case control morbidity, leukemia, occupational	Matched on Age and year of registration	6 radio/TV repair, males	New Zealand cancer registry
Pearce [85]	Case control, morbidity, leukemia, occupational	Age	12 radio/TV repair, males	New Zealand Cancer Registry
Szmigielski [37]	Cohort, morbidity, all types, occupational	Age, diagnosis date	128,000 total 3,700 exposed, males	Military's health departments, hospitals, medical board, safety groups operating as health hygienic service
Szmigielski [38]	Cohort morbidity all types, occupational	Age	124,500 total, about 3500-4500 exposed males	Polish army, service records listing of exposures
Thomas [86]	Case control, mortality, brain tumor, occupational	Educational level, match on age at death, year of death and area of residence. Risk factors of brain tumor	821 death certificates, males	Northern New Jersey, Philadelphia, PA, and southern Louisiana. Brain tumors verified through a hospital record review
Tynes [87]	Cohort morbidity, all types, occupational	Sea related lifestyle factors: A diet rich in fat, artificial light, disturbances in the geomagnetic field, alcohol	2619 females	National Cancer Registry of Norway
Wolf [17]	Cohort morbidity all sites, environmental	Socioeconomic class employment status, demographic heterogeneity due to differences in age gender and ethnicity	1844	Medical clinics, national and city incidence rate
Wright [28] Letter	Proportional Incidence Ratio (PIR) leukemia, occupational	Specific for age, gender and race	1 no. of cases (TV and radio repair)	Cancer Surveillance Program information on Los Angeles County

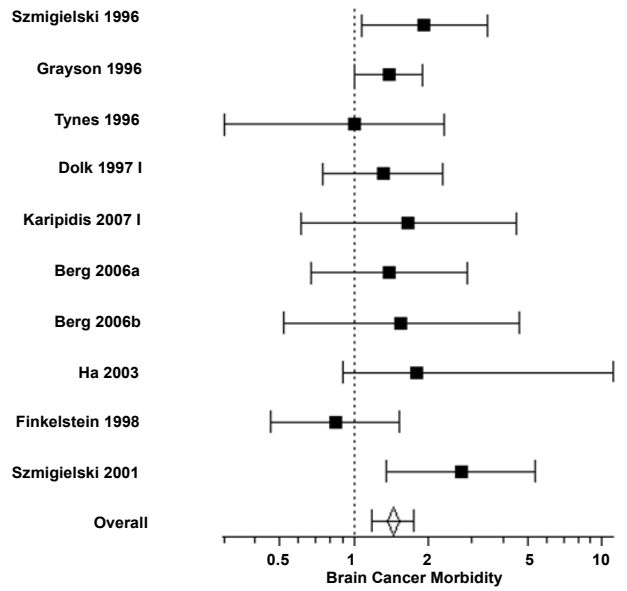

Figure 1: Cancer of the Brain and Central Nervous System Morbidity.
Risk of brain and central nervous system cancer was found to increase in relation to MW/RF radiation exposure

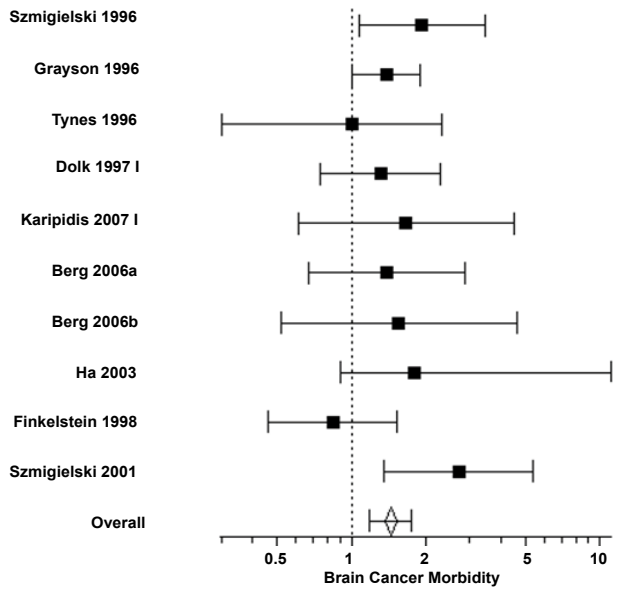

Figure 2: Lymphoma Morbidity
Risk of lymphoma increased in relation to MW/RF radiation exposure

childhood leukemia overall ratio OR = 1.35 (95% CI 1.17, 1.56), brain and CNS cancer morbidity OR = 1.44 (95% CI 1.18, 1.74), (Figure 1), lymphoma OR = 1.55 (95% CI 1.22, 1.97), (Figure 2), melanoma 1.47 (95% CI 1.24, 1.74), (Figure 3), adult leukemia OR = 1.24 (95% CI 1.12, 1.37), (Figure 4), breast cancer morbidity OR=1.23 (95% CI 1.10, 1.39).

Table 2 reports statistically significant increased risk for lymphoma morbidity, childhood leukemia morbidity, all leukemia adult morbidity, all leukemia adult mortality, melanoma morbidity, breast cancer morbidity, brain and CNS cancer morbidity, all cancer sites morbidity. For testicular cancer, borderline significant morbidity risk was found. No statistically significant association was found for brain and central nervous system (CNS) tumors morbidity in children, lymphoma and multiple myeloma mortality, and mortality from brain and CNS tumors. For all cancer sites mortality reduced risk was found, on the basis of 2 results that showed reduced risk and 5 results that showed increased risk.

Studies that indicated a promotional effect of MW/RF radiation exposure on cancer and a higher risk of cancer inverse with age

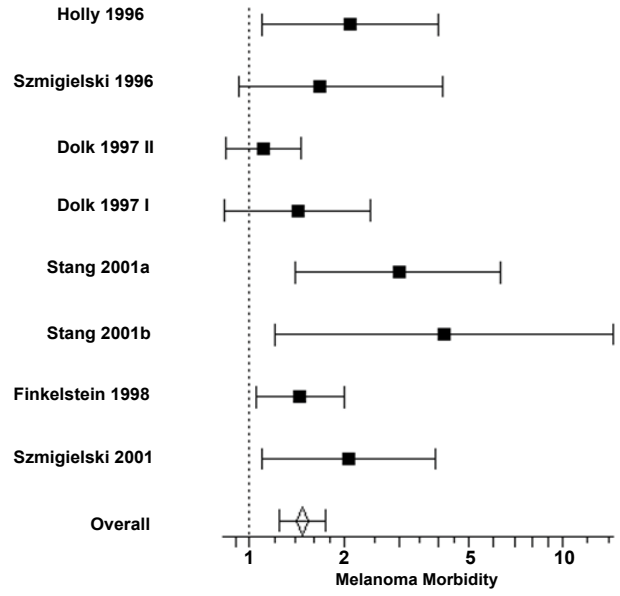

Figure 3: Melanoma Morbidity
Risk of melanoma increased in relation to MW/RF radiation exposure

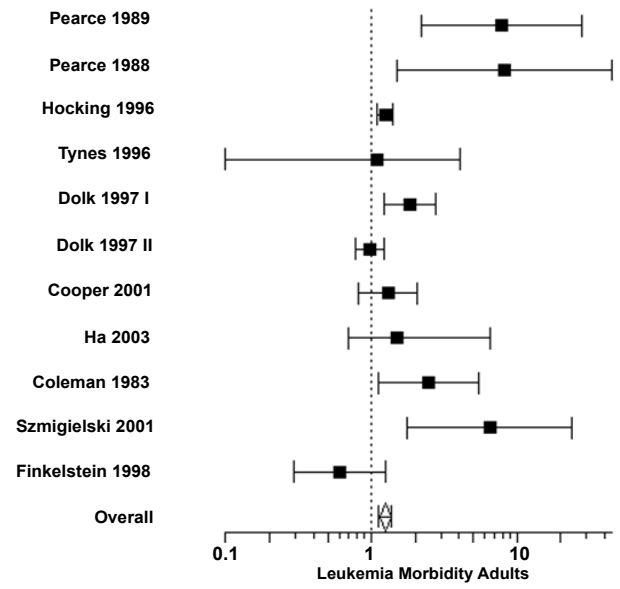

Figure 4: Leukemia Morbidity Adults
Risk of leukemia increased in relation to MW/RF radiation exposure

(younger have higher risk) are reported in table 3. Occupational military studies found increased risk of cancer mortality or morbidity with decreasing age [35-38]. There was higher risk of all cancer sites for the age groups 20-39 compared to older age groups [37] and latency period shortened in exposed vs. non exposed [38]. Environmental studies found indications for promotional effect (acceleration) and higher risk in younger age, with regard to cancer morbidity, mortality and survival.

In a study from Germany, the average age of developing cancer was 8.5 years earlier in the exposed vs. the non exposed population. For breast cancer, the average age in the exposed area was approximately 13 years younger than the average age of developing cancer in the exposed, and approximately 20 years less than in the non exposed population, as well as 12 years younger than the national average age for developing breast cancer in Germany [16]. An Israeli study on exposure to cell towers, found an extremely short latency period [17]. Risk increased and survival decreased for exposed vs. non exposed in children [39]. In a study from Korea, higher risk was found under 30 years old [40].

Table 2: Results of meta analysis

Cancer type	Fixed effect model Overall Ratio
All cancer sites morbidity children and adults together	*1.07 (90% CI 1.04, 1.10 (95% CI 1.03, 1.11) (99% CI 1.02, 1.12)
All cancer sites morbidity adults	*1.11 (90% CI 1.06, 1.15) (95% CI 1.06, 1.16) (99% CI 1.04, 1.18)
All cancer sites mortality children and adults	0.92 (90% CI 0.89, 0.96) (95% CI 0.88, 0.97) (99% CI 0.87, 0.98)
All cancer sites mortality adults	0.92 (90%CI 0.88, 0.96) (95%CI 0.88, 0.97) (99%CI 0.86, 0.98)
Lymphoma morbidity	*1.55 (90% CI 1.27, 1.90) (95% CI 1.22, 1.97) (99% CI 1.14, 2.12)
Lymphoma and multiple myeloma mortality	1.17 (90% CI 0.99, 1.38) (95% CI 0.96, 1.42) (99% CI 0.91, 1.51)
Childhood leukemia morbidity	*1.35 (90% CI 1.20, 1.53) (95% CI 1.17, 1.56) (99% CI 1.12, 1.64)
All leukemia morbidity adults	*1.24 (90%CI 1.14, 1.35) (95%CI 1.12, 1.37) (99%CI 1.09, 1.42)
All leukemia mortality adults	*1.29 (90% CI 1.16, 1.44) (95% CI 1.13, 1.47) (99% CI 1.09, 1.53)
Melanoma morbidity	*1.47 (90% CI 1.27, 1.69) (95% CI 1.24, 1.74) 99%) CI 1.18, 1.83)
Breast cancer morbidity	*1.23 (90% CI 1.12, 1.36) (95% CI 1.10, 1.39) (99% CI 1.06, 1.44)
Brain (and CNS) cancer morbidity	*1.44 (90% CI 1.22, 1.69) (95% CI 1.18, 1.74) (99% CI 1.11, 1.85)
Brain (and CNS) cancer mortality	1.18 (90% CI 0.97, 1.43) (95% CI 0.94, 1.48) (99% CI 0.87, 1.59)
Brain cancer morbidity in children	1.11 (90% CI 0.97, 1.28) (95% CI 0.94, 1.32) (99% CI 0.90, 1.39)
Testicular cancer morbidity	1.24 (90% CI 1.03, 1.50) ** (95% CI 0.99, 1.56) (99%CI 0.92, 1.67)

* Statistically significant

** Borderline significant

Discussion

To the best of our knowledge, our study is the first meta-analysis focusing on the association between exposure to MW/RF

Table 3: Promotional effect and higher risk for young vs. older ages

Study	Effect
Degrave [35]	RR = 1.23 (95% CI 1.03- 1.47) Indication that cancer death rate ratio increased with decreasing age (p = 0.004)
Szmigielski [37]	The risk of leukemia and lymphoma for younger people was 8 fold more than expected p < 0.01. There was higher risk of all site cancers in the age groups of 20- 29 and 30-39 (p < 0.05), compared to older age groups. The risk reduced with increasing age
Szmigielski [38]	All site cancers-curve showed shorter latency period in the exposed group vs. the non-exposed by 5-10 years, which could related to at least one type of cancer. Haematologic/lymphatic cancers-curves showed a considerable increment in the number of cases in exposed group aged above 40 years, and for these types of cancer the curves show early age of victims
Robinette (1980) analyzed by Goldsmith [36]	For the aviation technicians group, that had the highest exposure, death rates were significantly higher than those for the remaining men for all deaths, disease-related deaths, deaths from malignance and deaths from malignancy of the lymphatic and hematopoietic systems. The same group had a younger mean age (23.4) than the average for aviation electrician's mates AE (24.7), a category that showed no increase in deaths from any malignancy or from other diseases
Park [40]	Higher risk of mortality from leukemia and multiple myeloma in people under 30 years old compared to other age groups
Hocking [39]	Increased incidence and decreased survival among children who resided near TV transmitters, supported the possibility that RFR acts as a facilitator of cancer
Eger [16]	Average age of developing cancer was 64.1 years in the inner area (exposed) and 72.6 years in the outer area, a difference of 8.5 years. The average age of patients that developed breast cancer in the inner area was 50.8 years. In the outer area the average age was 69.9 years, approximately 20 years less. In Germany the average age for developing breast cancer is about 63 years.
Wolf [17]	The authors suggested a strong cancer promoting effect at very low radiation, because the study found an extremely short latency period of less than 2 years. According to the authors, this short latency period indicated, that if there is a causal association between RF/MW radiation emitted from base stations and cancer as they believe, then there is a very strong promotional effect at low levels of exposure

radiation and cancer risk. Our results are consistent with the review by Yekymenko et al. [6] and (Levitt and Lai 2010) [9], who revealed evidence about increased risk of cancer associated with exposure to MW/RF radiation. Reviews by Elwood [10], Breckenkamp et al. [12] and Ahlbom [11], who found that evidence for cancer associated with MW/RF radiation was inconsistent just a decade ago, were published before more up to date results on increased risk of all site cancers were published [16,17,31,41], as well as specific cancer studies [35,42]. Other researchers have recognized the need for a more precautionary approach vs. the current standards, after taking into account recent data [6,8,13,14]. According to Carpenter [13,14], leukemia is the cancer most likely to indicate elevated risk from whole body exposure to electromagnetic fields (EMFs) of any frequency, since the same cancer is elevated following exposure to power-line frequencies.

Meta analyses and reviews may be complementary one to one each other, but serve an important purpose in contrasting or combining results from other studies, in an effort to identify patterns and sources of conflict between their results, or patterns of intriguing relationships that may come to light in the context of multiple studies [19]. While a review helps to explain results in terms of biology and bias, quantitative analysis has more precision with small but important associations or subtle patterns in the material [19]. We detected the main patterns and biases in the body of evidence during the preparation of this work. In environmental studies: ecological bias, i.e., without unique information on exposure levels, the use of an average exposure measure; the use of distance vs. radiation exposure. In occupational studies: the healthy worker effect bias, involvement of other risk factors that can act in synergy or mask the risk without a separate analysis. In both occupational and environmental studies, confounder analysis was lacking at the individual level. Despite the limitations of individual studies, an increased risk was found for several types of cancer. Though brain cancer morbidity was elevated (1.11) for childhood brain tumors, it was not statistically significant. The lack of a sufficient latency period may be the reason. In a recent review on ionizing radiation-induced malignant gilomas, brain tumors occurred within 15 years in 82% of the patients and in 18% of the patients they developed > 15 years after radiation therapy [43]. Only 26 cases of radiation-associated meningiomas occurring in the pediatric population have been reported in the English literature, they are very rare [44]. In one study meningioma following radiation therapy occurred after 6-13 years and in other studies after a latency period of 3-63 years [44]. The association for brain tumor morbidity was received after conservative analysis, i.e., it did not include risk results [45] from low power transmitters. After we removed the breast cancer mortality category because of too few studies for analysis, a correlation was found [40,46,47]. No correlation was found for lymphoma mortality on the basis of the low number of studies. Borenstein et al. [33] and Abramson [32], both experts of meta-analyses, related to the common criticism on meta analyses about comparing diverse studies, using different methodologies. They disagree that it is necessarily a disadvantage. According to Abramson [32], diverse studies may help to explain differences in results and provide useful additional information. Such comparisons may be the main purpose of a meta-analysis and can be the power that drives the study in the sense of understanding the phenomenon. Heterogeneity can be seen as an opportunity rather than a problem. Pooling of results may reveal an effect that individual trials do not clearly show and it may also indicate that results seen in isolated trials may be a false/positive caused by random error [32].

Supporting evidence for promotional effects and higher risk for young ages

Findings of Tillmann et al. [48] were recently confirmed in a study by Lerchl et al. [49]. In that study, mice exposed in the womb to a cancer agent and then exposed to a cell phone signal, had significantly higher rates of liver and lung tumors, as well as lymphoma compared to the cancer agent without the cell phone signal. This study employed radiation levels that do not cause thermal reactions and are well below current safety standards. The current standards are designed for prevention of an acute/immediate effect of heat damage (thermal effect) from short term exposure whereas the entire population is exposed for years/life-time (long-term/chronic exposure) which standards state are not applicable. In a study that evaluated the effect of 900 MHz generated by mobile base stations on hematological parameters and cellular composition of bone marrow in mature and immature rats, exposure to a mobile base station was found to have a deleterious effect on hematological parameters and bone marrow composition; this effect was more severe in immature animals [50]. Brautbar [51] reported a rapid development of brain tumors in two cell phone testers with occupational exposure to cell phones and testing equipment, in whom brain tumors appeared within less than 5 years of the first exposure, and on the same side of the head that the phones were used. Richter et al. [52] reported a short latency period of brain tumors with occupational exposure to cell phones, suggesting that earlier-reported individual cases characterized by short latencies in young persons with high military occupational exposure, serve as predictors of increased group risk for exposures to RF/MW radiation. Earlier findings [53] suggested that young persons exposed to high levels of MW/RF radiation for long periods were at increased risk of cancer. In the Hardell group's studies on the possible association between brain tumors and mobile/ cordless telephone use, the highest risks were associated with > 5-year latency period in the 20-29-year age group (OR = 4.30, 95% CI = 1.22-15) for cordless phones [54], and the risk of astrocytoma grade I-IV was highest for cases with first use < 20 years of age, for mobile phone OR = 5.2 (95% CI = 2.2-12) and cordless phone OR = 4.4 (95% CI=1.9-10) [55].

Considering that the mankind is exposed to this radiation increasingly from multiple sources, with multiple ambient frequencies, on a daily basis, especially considering that this new combination of frequencies has not been studied (4G, together with smart meters, Wi-Fi, together with previous cellular generations that are currently in use), it is imperative to build revised measures in the current standards, taking into account the reality of chronic exposure and providing robust protection to the public.

Conclusions

Accumulated empirical evidence to date and summarized in this analysis using meta-analysis tools, found an increased risk of morbidity and/or mortality from lymphoma, leukemia, melanoma and brain/CNS cancers, following exposure to MW/RF radiation. Evaluating this evidence, current standards are clearly not sufficient to protect the public and workers from exposure to MW/RF radiation and should take into account long term effect of increased risk of cancer. Promotional effects and special sensitivity in young people supports the restriction of exposure in children to wireless technologies including Wi-Fi in schools. Exposure assessment limitations in empirical studies also postulate an under-estimation of the level of risk. It is crucial that future studies take into account individual specific data, both on confounders and exposures.

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Conflicts of interests

none

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