Evaluation of the literature on high-voltage power lines and neurodegenerative diseases

No. 2022/13Ae, The Hague, 29 June 2022

Background document to:
Power lines and health: neurodegenerative diseases
No. 2022/13e, The Hague, 29 June 2022

Gezondheidsraad

Contents

1 Introduction

In this background document to the advisory report *High-voltage power lines and health: neurodegenerative* diseases, drafted by the Electromagnetic Fields Committee of the Health Council, chapter 2 describes the search strategies the Committee has used for the various diseases and how relevant papers have been selected.
In chapter 3, the Committee describes the protocol it followed in order to analyse the data.
Chapter 4 sets out the criteria for assessing the strength of evidence for a causal relationship.
Chapter 5 contains explanatory notes on how to read the forest plots that can be found in this background document.
Chapter 6 features tables summarising the key data for all relevant papers by topic.
Finally, in chapter 7 the Committee describes the meta-analyses it has carried out and presents the results.

2 Search strategy

2.1 Epidemiological research

Searches were performed in the PubMed and EMF Portal databases for publications on epidemiological research into the various neurodegenerative diseases and exposure to extremely low frequency (ELF) magnetic fields or distance to high-voltage power lines. Only the most complete database, EMF Portal, was searched for experimental studies. Additional information on the search strategy for each disease is provided below: the search terms, the date the search was performed and the number of papers found. A number of papers were also obtained via other sources: reviews, reference lists and own literature collections. The papers found were selected for further analysis based on title. The relevant information was retrieved and transferred to an Excel file. In a number of cases, examination of the full text revealed that some publications did not contain the information sought or the research did not meet the criteria for inclusion in the analysis (see the protocols in chapter 3). The final number of papers included in the analyses is stated. The relevant information from these papers can be found in the tables in chapter 4, which also features tables showing the papers excluded and the reason for exclusion.

2.2 Amyotrophic lateral sclerosis (ALS)

Exposure to magnetic fields

PubMed

Searched for: ("extremely low frequency" OR "magnetic fields" OR "power line" OR "power lines" OR ELF) NOT (epithelial lining fluid OR ELF-phosphatase) AND (ALS OR amyotrophic OR motor neuron) AND epidemiol*.
Performed on 01-05-2019 with an update on 21-04-2021. Found: 42 papers. Selected based on title: 20 papers.

EMF Portal

Searched for: Keyword: amyotrophic lateral sclerosis; Topic: Epidemiologic studies; Frequency range: Power frequencies (50/60 Hz); Time span: Complete time span
Performed on 22-07-2019 with an update on 21-04-2021. Found: 40 papers. Not in PubMed: 13 papers.

Other sources (reference lists in reviews): 5 papers.

Total full text analysis: 38 papers. Criteria for inclusion in analysis not met: 14 papers. Considered in the report: 24 papers, of which 20 occupational exposure and 4 residential exposure.

Distance to high-voltage power lines

PubMed

Searched for: ("extremely low frequency" OR "magnetic fields" OR "power line" OR "power lines" OR ELF) NOT (epithelial lining fluid OR ELF-phosphatase) AND (ALS OR amyotrophic) AND distance AND epidemiol*.

Performed on 01-05-2019 with an update on 23-07-2020. Result: 5 papers. Selected based on title: 5 papers.

Other sources (reference lists in reviews): 1 article.

Total full text analysis: 6 papers. Criteria for inclusion in analysis not met: 0 papers. Considered in the report: 6 papers.

2.2.1 Alzheimer's disease

Exposure to magnetic fields

PubMed

Searched for: ("extremely low frequency" OR "magnetic fields" OR "power line" OR "power lines" OR ELF) NOT (epithelial lining fluid OR ELF-phosphatase) AND (alzheimer* OR dementia) AND epidemiol*

Performed on 01-05-2019 with an update on 21-04-2021. Result: 47 papers. Selected based on title: 15 papers.

EMF Portal

Searched for: Keyword: Alzheimer's disease; Topic: Epidemiologic studies; Frequency range: Power frequencies (50/60 Hz); Time span: Complete time span.

Performed on 22-07-2019 with an update on 21-04-2021. Result: 41 papers. Not in PubMed: 13 papers.

Other sources (reference lists in reviews): 2 papers.

Total full text analysis: 28. Criteria for inclusion in analysis not met: 10 papers. Considered in the report: 18 papers, all occupational exposure.

Distance to high-voltage power lines

PubMed

Searched for: ("extremely low frequency" OR "magnetic fields" OR "power line" OR "power lines" OR ELF) NOT (epithelial lining fluid OR ELF-phosphatase) AND (alzheimer* OR dementia) AND distance AND epidemiol*.

Performed on 01-05-2019 with an update on 23-07-2020. Result: 3 papers. Selected based on title: 3 papers.

Total full text analysis: 3 papers. Criteria for inclusion in analysis not met: 0 papers. Considered in the report: 3 papers.

2.2.2 Parkinson's disease

Exposure to magnetic fields

PubMed

Searched for: ("extremely low frequency" OR "magnetic fields" OR "power line" OR "power lines" OR ELF) NOT (epithelial lining fluid OR ELF-phosphatase) AND (parkinson*) AND epidemiol*

Performed on 01-05-2019 with an update on 21-04-2021. Result: 20 papers. Selected based on title: 13 papers.

EMF Portal

Searched for: Keyword: Parkinson's disease; Topic: Epidemiologic studies; Frequency range: Power frequencies (50/60 Hz); Time span: Complete time span.

Performed on 22-07-2019 with an update on 21-04-2021. Result: 25 papers. Not in PubMed: 5 papers.

Other sources (reference lists in reviews): 11 papers.

Total full text analysis: 29. Criteria for inclusion in analysis not met: 14 papers. Considered in the report: 15 papers, of which 12 occupational exposure and 3 residential exposure.

Distance to high-voltage power lines

PubMed

Searched for: ("extremely low frequency" OR "magnetic fields" OR "power line" OR "power lines" OR ELF) NOT (epithelial lining fluid OR ELF-phosphatase) AND (parkinson*) AND distance AND epidemiol*.

Performed on 01-05-2019 with an update on 23-07-2020. Result: 3 papers. Selected based on title: 3 papers.

Total full text analysis: 3 papers. Criteria for inclusion in analysis not met: 0 papers. Considered in the report: 3 papers.

2.2.3 Multiple sclerosis (MS)

Exposure to magnetic fields

PubMed

Searched for: ("extremely low frequency" OR "magnetic fields" OR "power line" OR "power lines" OR ELF) NOT (epithelial lining fluid OR ELF-phosphatase) AND (MS OR multiple sclerosis) AND epidemiol*
Performed on 04-05-2021. Result: 27 papers. Selected based on title: 5 papers.

EMF Portal

Searched for: Keyword: Multiple sclerosis; Topic: Epidemiologic studies; Frequency range: Power frequencies (50/60 Hz); Time span: Complete time span.
Performed on 04-05-2021. Result: 7 papers. Not in PubMed: 0 papers.

Other sources (reference lists in reviews): 0 papers.

Total full text analysis: 5. Criteria for inclusion in analysis not met: 0 papers. Considered in the report: 5 papers, of which 3 occupational exposure and 2 residential exposure.

Distance to high-voltage power lines

PubMed

Searched for: ("extremely low frequency" OR "magnetic fields" OR "power line" OR "power lines" OR ELF) NOT (epithelial lining fluid OR ELF-phosphatase) AND (MS OR multiple sclerosis) AND distance AND epidemiol*.
Performed on 04-05-21. Result: 2 papers. Selected based on title: 2 papers.

Total full text analysis: 2 papers. Criteria for inclusion in analysis not met: 0 papers. Considered in the report: 2 papers.

2.3 Experimental research

2.3.1 Amyotrophic lateral sclerosis (ALS)

EMF Portal

Searched for: Keyword: amyotrophic lateral sclerosis; Topic: Experimental studies; Frequency range: Power frequencies (50/60 Hz); Time span: Complete time span.
Performed on 29-06-2021. Result: 3 papers.

Selected based on title: 3 papers. Total full text analysis: 3. Not relevant: 0 papers. Considered in the report: 3 papers.

2.3.2 Alzheimer’s disease

EMF Portal

Searched for: Keyword: Alzheimer's disease; Topic: Experimental studies; Frequency range: Power frequencies (50/60 Hz); Time span: Complete time span.
Performed on 29-06-2021. Result: 19 papers.

Selected based on title: 19 papers. Total full text analysis: 19. Not relevant: 6 papers. Considered in the report: 13 papers.

2.3.3 Parkinson’s disease

EMF Portal

Searched for: Keyword: Parkinson 's disease; Topic: Experimental studies; Frequency range: Power frequencies (50/60 Hz); Time span: Complete time span.
Performed on 29-06-2021. Result: 8 papers.

Selected based on title: 8 papers. Total full text analysis: 8. Not relevant: 1 article. Considered in the report: 7 papers.

2.3.4 Multiple sclerosis (MS)

EMF Portal

Searched for: Keyword: multiple sclerosis; Topic: Experimental studies; Frequency range: Power frequencies (50/60 Hz); Time span: Complete time span.
Performed on 28-07-2021. Result: 1 article.

Selected based on title: 0 papers. Considered in the report: 0 papers.

3 Protocol for the systematic analysis of epidemiological data

Searches occupational and residential exposure:

- Search PubMed using (without time limit) for
  - ALS: ("extremely low frequency" OR "magnetic fields" OR "power line" OR "power lines" OR ELF) NOT (epithelial lining fluid OR ELF-phosphatase) AND (ALS OR amyotrophic OR motor neuron) AND (epidemiol*)
  - Alzheimer: ("extremely low frequency" OR "magnetic fields" OR "power line" OR "power lines" OR ELF) NOT (epithelial lining fluid OR ELF-phosphatase) AND (alzheimer* OR dementia) AND (epidemiol*)
  - Parkinson: ("extremely low frequency" OR "magnetic fields" OR "power line" OR "power lines" OR ELF) NOT (epithelial lining fluid OR ELF-phosphatase) AND (parkinson*) AND (epidemiol*)
  - MS: ("extremely low frequency" OR "magnetic fields" OR "power line" OR "power lines" OR ELF) NOT (epithelial lining fluid OR ELF-phosphatase) AND (MS OR multiple sclerosis) AND (epidemiol*)
- Additionally check EMF-portal (www.emf-portal.org) using ‘Amyotrophic lateral sclerosis’ or ‘Alzheimer’s disease’ or ‘Parkinson’s disease’ or ‘Multiple sclerosis’, ‘Power frequencies’, ‘Epidemiological studies’, ‘Complete time span’
- Check reference lists of other reviews

Selection of search results:

- Select relevant studies based on title
- Refine selection based on abstract or full text
- Selected studies will be categorized as occupational or residential studies

Inclusion criteria:

- Peer-reviewed publications in English, French, German
- Published until 21-04-2021
- If several reports were published on the same population, for each outcome only the most complete, preferentially the most recent, report will be included. Also when multiple studies were based on overlapping populations only the most relevant/complete study was included.

Exclusion criteria:

- Studies where the main study goals did not include assessment of the effect of ELF-MF exposure or electrical shock, or proxies of these such as electrical occupation and distance to power lines
- Studies on dementia only or on cognitive decline, i.e. without specification of Alzheimer
- Ecological studies
- Cross-sectional studies
- Studies with self-reported exposure to ELF MF
- Residential studies with measurements of less than 24 h

PECOS

Occupational exposure to ELF-MF

- ***P****articipants*: people that have been actually or likely exposed to ELF-MF above background levels during performance of their work duties, and people that have not been exposed above background levels during performance of their work duties
- ***E****xposures:*
  - exposure to ELF-MF above background levels as classified by a job-exposure matrix (JEM) or actual measurements or assessment by an occupational hygienist
  - working or having worked in a job that most likely involved exposure to ELF-MF above background levels (“electrical occupations”); exposure based on job title
- ***C****omparisons:* all analyses will be stratified according to study type: industrial cohort vs general population studies (cohort or case-control)
  - exposed vs non-exposed
    - all studies
    - only studies with complete work history
    - all studies stratified for incidence vs mortality
    - all studies stratified for exposure assessment method: JEM or actual measurements or assessment by an occupational hygienist vs job title
  - highest/longest vs non-exposed (if available)
  - exposure-response relations (if feasible)
    - ***O****utcomes*: ALS (or motor neuron disease) / Alzheimer / Parkinson (or Parkinsonism) / Multiple sclerosis
    - ***S****tudy design*: (nested) case-control, cohort

Exposure to electric shocks

- ***P****articipants*: people that have worked in a job with a risk of electric shocks, and people that have not worked in a job with a risk of electric shocks
- ***E****xposures*: working in a job with a risk of electric shocks

- ***C****omparisons*: all analyses will be stratified according to study type: industrial cohort vs general population studies (cohort or case-control)
  - ever vs never worked in job with a risk of electric shocks
- ***O****utcomes*: ALS (or motor neuron disease) / Alzheimer / Parkinson (or Parkinsonism) / Multiple sclerosis
- ***S****tudy design*: (nested) case-control, cohort

Residential exposure to ELF-MF
- ***P****articipants*: general population
- ***E****xposures*: measured or calculated exposure to ELF-MF or distance to the nearest overhead power line (used as a proxy for exposure to ELF-MF generated by the power line)
- **C**omparisons: All analysis will be stratified for exposure to power lines only vs exposure to all sources of ELF-EMF
  - Exposed vs lowest
    - All studies
      - Mortality vs incidence
      - Stratified for exposure assessment method: measured, modelled, distance to power line (categories 0-50, 50-200, 200-400/600 or >400/600 m)
      - Highest/longest vs lowest
- ***O****utcomes*: ALS (or motor neuron disease) / Alzheimer / Parkinson (or Parkinsonism) / Multiple sclerosis
- ***S****tudy design*: (nested) case-control, cohort

Data extraction:
- First author, year of publication
- Study population: general population (residential studies) or workers (occupational studies)
- Study design: (nested) case-control, cohort, cross-sectional
- Calendar years during which subjects were included in the study
- Details of the assessment of exposure (both for ELF-MF and electric shocks) (occupational: case-by-case assessment by expert, JEM; occupational and residential: measurements, calculations, distance)
- Recording of occupational history, e.g. last-held job, or longest held job, or job from registry or census data, completeness of job history
- Case-control studies: selection of controls and whether cases and controls come from the same population at risk
- Residential studies: exposure assessment at one or multiple addresses (completeness of exposure history)

- Type of outcome (incidence, mortality)
- Outcome assessment
- In mortality studies: was outcome the primary cause of death or registered anywhere on the death certificate
- Total numbers of cases / controls, deaths
- Risk estimates of all reported ELF-MF exposure categories for all exposure durations; if risk estimates are available for ELF-MF exposure and for (groups of) electrical occupations, extract separately
- If available, both crude and adjusted risk estimates
- Confounding factors used for adjustment of risk estimates

In case of doubt, discuss and resolve questions in Committee

Research aims (for each disease) for occupational studies:
- Primary objectives:
  - Assess the association between (a proxy for) the exposure to ELF-MF and the incidence of, or death from, the disease
  - Assess the association between (the risk of) electric shocks and the incidence of, or death from, the disease
  - Assess whether there is an increasingly stronger association between the incidence of, or death from, the disease with increasing level of exposure to ELF-MF
- Secondary objectives:
  - Assess whether there is a different association with (a proxy for) exposure to ELF-MF for studies that report the incidence of the disease (morbidity) vs studies that report the disease as a cause of death (mortality)
  - Assess whether there is a different association between (a proxy for) exposure to ELF-MF and the incidence of, or death from, the disease in studies with a more complete occupational history vs studies that have an incomplete occupational history
  - Assess whether there is a different association between the incidence of, or death from, the disease and occupations for which exposure characterization has been done by JEM or actual measurements or assessment by an occupational hygienist vs exposure characterization by job title

Research aims (for each disease) for residential studies:

- Primary objectives:
  - Assess whether there is an association between the distance to power lines and the incidence of, or death from, the disease
  - Assess whether there is an association between the measured or calculated ELF-MF exposure level and the incidence of, or death from, the disease

Analyses:

- For each meta-analysis, there should be at least three studies from which data can be used, otherwise only the results of the individual studies will be reported
- If in a study only effect risk estimates for males and females separately are given, a pooled risk estimate for both sexes combined will be calculated using a fixed-effects-within-study meta-analysis
- Ever vs never exposed:
  - If in a study risk estimates for two or more ELF-MF exposure levels compared to a reference level are given, a pooled risk estimate for all exposure categories will be calculated using a fixed-effects-within-study meta-analysis
  - Random effects meta-analysis will be used to calculate summary risk estimates stratified for the categories defined above
- Longest / highest exposed:
  - Summary risk estimates will be calculated for all highest / longest / highest longest exposure categories for studies with more than two exposure categories (including the reference category) using random effects meta-analysis
- Meta-regression will be used to assess exposure-response relations based on data from studies with quantitative ELF-MF exposure, where exposure is expressed in microtesla (μT)
- To assess heterogeneity, I^2 and the between-study standard deviation tau^2 will be calculated
- Meta-regression will be used if necessary and feasible to explain heterogeneity
- Forest plots will be made.

4 Criteria for the classification of strength of evidence for a causal relationship

The Committee applies the US Environmental Protection Agency (EPA)[1] methodology when assessing strength of evidence for a causal relationship, which uses the following classifications:

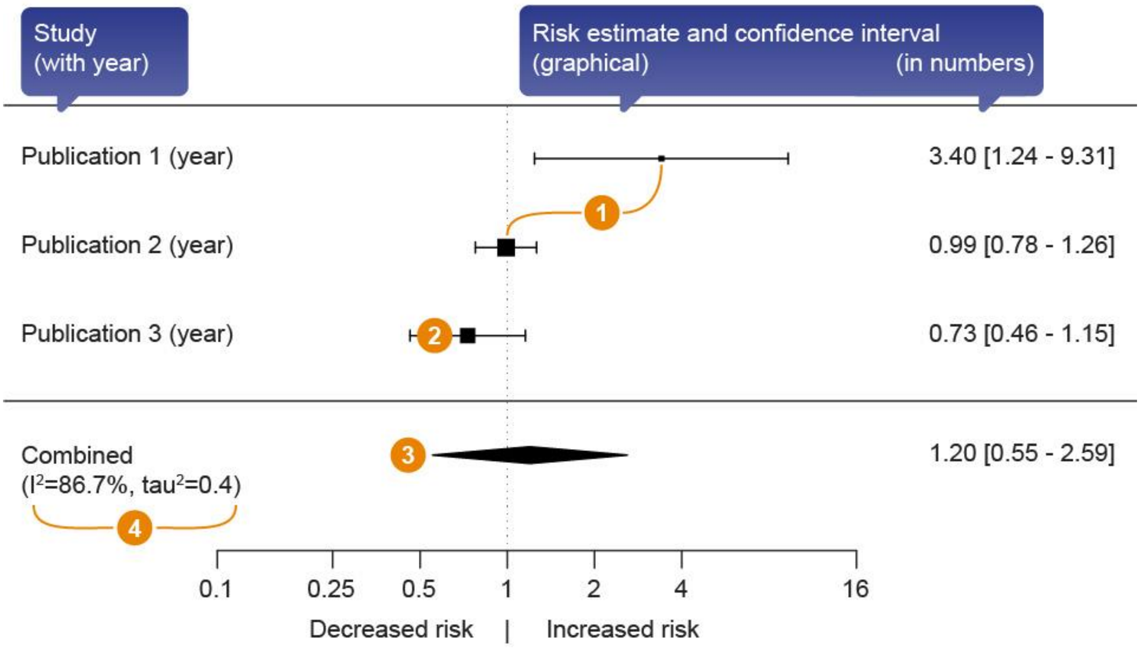
Value as evidence of a causal relationship	Description of associated evidence
Causal relationship proven	Evidence is sufficient to conclude that there is a causal relationship with relevant exposures. Multiple high-quality studies conducted by multiple research groups in which chance, confounding, and other biases could be ruled out with reasonable confidence have shown health effects. Such studies include controlled human exposure studies or observational studies that are supported by other lines of evidence (e.g., animal studies or mode of action information).
Causal relationship likely	Evidence is sufficient to conclude that a causal relationship is likely to exist. Multiple high-quality studies where results are not explained by chance, confounding, and other biases have shown health effects, but uncertainties remain in the evidence overall. For example: observational studies show an association, but exposures to other agents are difficult to address and/or other lines of evidence (controlled human exposure, animal, or mode of action information) are limited or inconsistent. Or animal toxicological evidence from multiple studies from different laboratories demonstrate effects, but limited or no human data are available.
Suggestive of a causal relationship	Evidence is suggestive of a causal relationship but is limited, and chance, confounding, and other biases cannot be ruled out. For example: at least one high-quality epidemiologic study shows an association and/or at least one high-quality animal study shows effects relevant to humans. Or, when the body of evidence is relatively large, evidence from studies of varying quality is generally supportive but not entirely consistent.
Inadequate to infer a causal relationship	Evidence is inadequate to determine that a causal relationship exists. The available studies are of insufficient quantity, quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of an effect.
Not likely to be a causal relationship	Several adequate studies, covering the full range of levels of exposure that human beings are known to encounter and considering at-risk populations and lifestages, are mutually consistent in not showing an effect at any level of exposure.

5 Explanatory notes on forest plots

In this advisory report, the results of the meta-analyses are presented in 'forest plots'. These graphs show the risk estimate and confidence interval both for each individual study and the combined result of the meta-analysis. The symbol (the small square in the figure below) shows the mean value for the individual studies. The size of the symbol represents the weighting factor, which is related to the number of people in the study: the more people and the bigger the symbol, the greater the contribution of the study towards the combined result. The horizontal lines show the 95% confidence interval, which is a measure of the precision of the risk estimate. The diamond shows the risk estimate with confidence interval for the combined effect. I^2 and tau^2 are measures of heterogeneity. The greater the heterogeneity, the less value can be attributed to the result of the meta-analysis.

Explanation: a forest plot

The results of the meta-analyses are presented in this advisory report in so-called forest plots. These show the risk estimate and confidence interval of both each individual study and the combined result of the meta-analysis.



1 Square
The location indicates the risk estimate, the size indicates the number of subjects in the study as well as the contribution to the combined result.

2 Horizontal line
The horizontal line indicates the confidence interval.

3 Diamond
The diamond shape indicates the risk estimate with confidence interval for the combined result.

4 I^2 en tau^2
I^2 en tau^2 are measures of the heterogeneity of the results of the individual studies.
The more the heterogeneity, the less value can be given to the results of the meta-analyses.

Figure 1 Example forest plot

6 Data summary

The tables below summarise the data from the studies included in the meta-analyses of the association between:

- ALS and residential exposure (6.1);
- ALS and occupational exposure to magnetic fields (6.2);
- ALS and occupational exposure to electric shocks (6.3);
- Alzheimer's disease and residential exposure (6.4);
- Alzheimer's disease and occupational exposure to magnetic fields (6.5);
- Parkinson's disease and residential exposure (6.6);
- Parkinson's disease and occupational exposure to magnetic fields (6.7);
- MS and occupational exposure to magnetic fields (6.8).

A list of studies that were not included in the meta-analyses and the reason for exclusion is also provided in each case.

6.1 Amyotrophic lateral sclerosis (ALS) and residential exposure

Table 1 Studies of the association between residential exposure and risk of ALS that were included in the analysis

Reference	Country, period	Type of study, population, patients/controls	Exposure criterion	Disease, assessment	Risk estimate. In some cases the Committee has aggregated categories
Distance					
Huss 2009[2]	Switzerland 2000-2005	Cohort, general population	Distance from high-voltage power line	ALS Mortality	0-50 m: no OR 50-200 m: HR=0.85 (0.46-1.59) 200-600 m:HR=0.72 (0.52-1.00)
Marcilio 2011[3]	Brazil 2001-2005	Case-control, general population	Distance from high-voltage power line	ALS Mortality	Distance: 0-50 m: no OR 50-100 m: OR=0.49 (0.15-1.56) 100-200 m: OR=1.14 (0.65-2.02) 200-400 m: OR=1.24 (0.83-1.86) Magnetic field: No risk estimate (only 1 patient)

Frei 2013[4]	Denmark 1994-2011	Case-control, general population	Distance from high-voltage power line	MND Incidence	0-50 m: HR=0.8 (0.34-1.89) 50-200 m: HR=0.94 (0.66-1.32) 200-600 m: HR=0.97 (0.81-1.16)
Seelen 2014[5]	Netherlands 2006-2013	Case-control, general population	Distance from high-voltage power line	ALS Incidence	0-50 m (50-150 kV): OR=1.05 (0.40-2.75) 50-200 m (50-150 kV): OR=0.91 (0.60-1.37) 50-200 m (200-380 kV): OR=0.73 (0.15-3.5) 200-600 m (50-150 kV): OR=0.89 (0.69-1.14) 200-600 m (200-380 kV): OR=1.31 (0.79-2.18)
Vinceti 2017[6]	Italy 1998-2008	Case-control, general population	Distance from high-voltage power line Magnetic field	ALS Incidence	Distance: 0-50 m: OR=1.01 (.53-1.94) 50-200 m: OR=0.95 (0.67-1.34) 200-600 m: OR=0.72 (0.56-0.92)
Filippini 2021[7]	Italy 2002-2012	Case-control, general population	Distance from high-voltage power line	ALS Incidence	0-50 m: OR=1.3 (0.4-4.6) 50-200 m: OR=11.2 (1.3-98.4) 200-600 m: OR=4.4 (0.4-45.9)
Magnetic field					
Vinceti 2017[6]	Italy 1998-2008	Case-control, general population	Distance from high-voltage power line Magnetic field	ALS Incidence	Magnetic field: 0.1-<0.2 µT: OR=0.64 (0.14-2.85) 0.2-<0.4 µT: OR=1.17 (0.32-4.26) ≥0.4 µT: OR=0.27 (0.04-2.13)

Abbreviations: ALS: amyotrophic lateral sclerosis; HR: hazard rate; kV: kilovolt; MND: motor neuron disease; OR: odds ratio.

Table 2 Studies of the association between residential exposure and risk of ALS that were not included in the analysis

Reference	Reason for exclusion
Marcilio 2011[3]	No risk estimate for exposure to ELF magnetic fields (only 1 patient)
Das 2012[8]	No residential exposure to ELF magnetic fields assessed

6.2 Amyotrophic lateral sclerosis (ALS) and occupational exposure to magnetic fields

Table 3 Studies of the association between occupational exposure to magnetic fields and risk of ALS that were included in the analysis

Reference	Country, period	Type of study, population, patients/ controls	Exposure criterion	Disease, assessment	Risk estimate. In some cases the Committee has aggregated categories
General population					
Deapen 1986[9]	US 1977-1979	Case-control, general population	Occupation	ALS Incidence	Electrical occupation: OR=3.8 (1.4-13.0)
Gunnarsson 1991[10]	Sweden Registered in Sweden in 1960, alive in 1970	Case-control, general population	Occupation	ALS Mortality	Electrical occupation: OR=1.5 (0.9-2.6)
Gunnarsson 1992[11]	Sweden 1990	Case-control, general population	Occupational history	MND Incidence	Electrical occupation: OR=6.7 (1.0-32.1)
Davanipour 1997[12]	US ~1996	Case-control, general population	Occupational history	ALS Incidence	Average total exposure (0.31 µT): OR=1.70 (0.91-3.60)
Savitz 1998a[13]	US 1950-1986	Cohort, electricity companies	JEM	ALS Mortality	Ever increased exposure (calculated): RR =1.25 (0.58-2.67)
Savitz 1998b[14]	US 1985-1991	Case-control, general population	Death certificate	ALS Mortality	Ever increased exposure: OR=1.3 (1.1-1.6)
Noonan 2002[15]	US 1987-1996	Case-control, general population	JEM	ALS Mortality	Ever increased exposure (calculated): OR=0.91 (0.69-1.19)
Park 2005[16]	US 1992-1998	Case-control, general population	JEM	MND Mortality	Ever increased exposure: OR=0.94 (0.73-1.20)

Parlett 2011[17]	US 1979-1989	Cohort, general population	JEM	MND Mortality	Ever increased exposure (calculated): HR=0.99 (0.59-1.68)
Fischer 2015[18]	Sweden 1991-2010	Case-control, general population	JEM	ALS Incidence	Ever increased exposure (calculated): OR=0.98 (0.92-1.04)
Huss 2015[19]	Switzerland 2000-2008	Cohort, general population	JEM	ALS Mortality	Occupation in 1990, median exposure (calculated): HR=1.19 (1.02-1.40)
Vergara 2015[20]	US 1991-1999	Case-control, general population	JEM	MND Mortality	Ever increased exposure (calculated): OR=1.09 (1.01-1.17)
Koeman 2017[21]	Netherlands 1986-2003	Cohort, general population	JEM	ALS Mortality	Ever increased exposure (calculated): 1.92 (1.06-3.48)
Peters 2019[22]	Italy, Ireland, Netherlands 2006-2015	Case-control, general population	JEM	ALS Incidence	Ever increased exposure: OR=1.10 (0.95-1.28)
Chen 2021[23]	New Zealand 2013-2016	Case-control, general population	JEM	MND Incidence	Ever increased exposure: OR=0.77 (0.56-1.05)
Industrial populations					
Håkansson 2003[24]	Sweden 1985-1996	Cohort, engineering industry	JEM	ALS Mortality	Ever increased exposure (calculated): RR=1.82 (1.24-2.68)
Röösli 2007[25]	Switzerland 1972-2002	Cohort, railway workers	Measurements, modelling	ALS Mortality	Cumulative exposure > median: HR=2.32 (0.70-7.73)
Sorahan 2014[26]	England, Wales 1973-2010	Cohort, electricity companies	Occupational history	ALS Mortality	Ever increased exposure (calculated): RR=1.52 (1.08-2.13)
Pedersen 2017[27]	Denmark 1982-2010	Cohort, electricity companies	JEM	MND Mortality	Ever increased exposure (calculated): IRR=1.89 (0.83-4.33)

Abbreviations: ALS: amyotrophic lateral sclerosis; JEM: job-exposure matrix; HR: hazard rate; IRR: incidence rate ratio; MND: motor neuron disease; µT: microtesla; OR: odds ratio; RR: rate ratio.

Table 4 Studies of the association between occupational exposure to magnetic fields and risk of ALS that were not included in the analysis

Reference	Reason for exclusion
Buckley 1983[28]	No ELF exposure established a priori
Schulte 1996[29]	No ELF exposure established a priori
Strickland 1996[30]	No specifically exposed industries
McGuire 1997[31]	No specifically exposed industries
Johansen 1998[32]	Update in later publication
Johansen 2000[33]	Update in later publication
Feychting 2003[34]	Update in later publication
Weisskopf 2005[35]	Only specific occupations
Sorahan 2007[36]	Update in later publication
Sutedja 2007[37]	Insufficient information on type of work
Stampfer 2009[38]	Only specific occupations
Fang 2009[39]	Insufficient information on exposure

6.3 Amyotrophic lateral sclerosis (ALS) and occupational exposure to electric shocks

Table 5 Studies of the association between occupational exposure to electric shocks and risk of ALS that were included in the analysis

Reference	Country, period	Type of study, population, patients/controls	Exposure criterion	Disease, assessment	Risk estimate. In some cases the Committee has aggregated categories
Deapen 1986[9]	US 1977-1979	Case-control, general population	Occupation Risk of electric shock	ALS Incidence	Electric shock with loss of consciousness: OR=2.8 (1.0-9.9)
Gunnarsson 1992[11]	Sweden 1990	Case-control, general population	Occupational history	MND Incidence	Shock, low+high current (calculated): OR=1.06 (0.52-2.18)
Fischer 2015[18]	Sweden 1991-2010	Case-control, general population	JEM	ALS Incidence	Ever shock (calculated): OR=1.03 (0.96-1.10)
Huss 2015[19]	Switzerland 2000-2008	Cohort, general population	JEM	ALS Mortality	Ever shock: HR=0.97 (0.66-1.42)
Koeman 2017[21]	Netherlands 1986-2003	Cohort, general population	JEM	ALS Mortality	Ever shock (calculated): HR=1.23 (0.80-1.90)
Peters 2019[22]	Italy, Ireland, Netherlands 2006-2015	Case-control, general population	JEM	ALS Incidence	Ever shock: OR=1.19 (1.01-1.40)

Chen 2021[23]	New Zealand 2013-2016	Case-control, general population	JEM	MND Incidence	Ever shock: OR=1.35 (0.98-1.86)

Abbreviations: JEM: job-exposure matrix; HR: hazard rate; MND: motor neuron disease; OR: odds ratio.

Table 6 Studies of the association between occupational exposure to electric shocks and risk of ALS that were not included in the analysis

Reference	Reason for exclusion
Grell 2012[40]	Imprecise risk estimate (only 2 patients)

6.4 Alzheimer's disease and residential exposure

Table 7 Studies of the association between residential exposure and risk of Alzheimer's disease that were included in the analysis

Reference	Country, period	Type of study, population, patients/controls	Exposure criterion	Disease, assessment	Risk estimate
Distance					
Huss 2009[2]	Switzerland 2000-2005	Cohort, general population	Distance from high-voltage power line	Alzheimer's disease Mortality	0-50 m: HR=1.24 (0.80-1.92) 50-200 m: HR=1.13 (0.95-1.34) 200-600 m:HR=1.02 (0.90-1.11)
Frei 2013[4]	Denmark 1994-2011	Case-control, general population	Distance from high-voltage power line	Alzheimer's disease Incidence	0-50 m: HR=1.04 (0.69-1.56) 50-200 m: HR=0.95 (0.81-1.12) 200-600 m: HR=1.05 (0.98-1.13)
Gervasi 2019[41]	Italy 2011-2016	Case-control, general population	Distance from high-voltage power line	Alzheimer's disease Incidence	0-50 m: HR=1.11 (0.95-1.30) 50-200 m: HR=1.00 (0.92-1.09) 200-600 m: HR=1.01 (0.95-1.07)

Abbreviations: HR: hazard rate.

6.5 Alzheimer's disease and occupational exposure to magnetic fields

Table 8 Studies of the association between occupational exposure to magnetic fields and risk of Alzheimer's disease that were included in the analysis

Reference	Country, period	Type of study, population, patients/controls	Exposure criterion	Disease, assessment	Risk estimate. In some cases the Committee has aggregated categories
General population					
Sobel 1995[42]	Finland, US 1977-1993	Case-control, general population	Occupation, expert opinion	Alzheimer's disease Incidence	Ever increased exposure: OR=2.90 (1.60-5.40)
Savitz 1998b[14]	US 1985-1991	Case-control, general population	Death certificate	Alzheimer's disease Mortality	Ever increased exposure: OR=1.2 (1.0-1.4)
Feychting 1998[43]	Sweden 1989-1991	Case-control, general population	JEM	Alzheimer's disease Incidence	Ever increased exposure: OR=0.84 (0.40-1.79)
Graves 1999[44]	Canada 1987-1992	Case-control, general population	Occupation, expert opinion	Alzheimer's disease Incidence	Ever increased exposure, average score 2 experts (calculated): OR=0.83 (0.40-1.69)
Noonan 2002[15]	US 1987-1996	Case-control, general population	JEM	Alzheimer's disease Mortality	Ever increased exposure (calculated): OR=0.92 (0.78-1.08)
Feychting 2003[34]	Sweden 1981-1995	Cohort, general population	1970 occupation census, JEM	Alzheimer's disease Mortality	Ever increased exposure (calculated): RR=1.01 (0.93-1.10)
Harmanci 2003[45]	Turkey	Case-control, general population	Occupation, expert opinion	Alzheimer's disease Incidence	Ever increased exposure: OR=4.02 (1.02-15.78)
Qiu 2004[46]	Sweden 1987-1996	Cohort, general population	JEM	Alzheimer's disease Incidence	Ever increased exposure (calculated): OR=1.16 (0.91-1.48)
Park 2005[16]	US 1992-1998	Case-control, general population	JEM	Alzheimer's disease Mortality	Ever increased exposure: OR=1.12 (1.05-1.20)
Davanipour 2007[47]	US Up to 1999	Case-control, general population	Measurements, modelling	Alzheimer's disease Incidence	Ever increased exposure: OR=2.20 (1.20-3.90)
Seidler 2007[48]	Germany	Case-control, general population	Occupation, expert opinion	Alzheimer's disease Incidence	Ever increased exposure (calculated): OR=0.80 (0.49-1.33)
Andel 2010[49]	Sweden 1998-2001	Case-control, general population	JEM	Alzheimer's disease Incidence	Ever increased exposure (calculated): OR=1.37 (0.98-1.90)

Koeman 2015[50]	Netherlands 1986-2004	Case-control, general population	JEM	Non-vascular dementia Mortality	Ever increased exposure (calculated): HR=1.22 (1.07-1.40)
Industrial populations					
Savitz 1998a[13]	US 1950-1986	Cohort, electricity companies	JEM	Alzheimer's disease Mortality	Ever increased exposure (calculated): RR=1.72 (0.83-3.59)
Håkansson 2003[24]	Sweden 1985-1996	Cohort, engineering industry	JEM	Alzheimer's disease Mortality	Ever increased exposure (calculated): RR=2.15 (1.22-3.80)
Röösli 2007[25]	Switzerland 1972-2002	Cohort, railway workers	Measurements, modelling	Alzheimer's disease Mortality	Cumulative exposure > median: HR=2.56 (1.12-5.82)
Sorahan 2014[26]	England, Wales 1973-2010	Cohort, electricity companies	Occupational history	Alzheimer's disease Mortality	Ever increased exposure (calculated): RR=1.03 (0.80-1.33)
Pedersen 2017[27]	Denmark 1982-2010	Cohort, electricity companies	JEM	Alzheimer's disease Mortality	Ever increased exposure (calculated): IRR=0.97 (0.67-1.39)

Abbreviations: JEM: job-exposure matrix; HR: hazard rate; IRR: incidence rate ratio; OR: odds ratio; RR: rate ratio.

Table 9 Studies of the association between occupational exposure to magnetic fields and risk of Alzheimer's disease that were not included in the analysis

Reference	Reason for exclusion
Sobel 1996[51]	Update in later publication
Salib 1996[52]	No exposure to ELF magnetic fields determined
Schulte 1996[29]	Only specific occupations, not selected a priori for ELF exposure
Johansen 1998[32]	Update in later publication
Johansen 2000[33]	Update in later publication
Li 2002[53]	No Alzheimer's disease
Sorahan 2007[36]	Update in later publication
Stampfer 2009[38]	Only specific occupations
Grell 2012[40]	Incomplete records of shocks
Davanipour 2014[54]	No Alzheimer's disease

6.6 Parkinson's disease and residential exposure

Table 10 Studies of the association between residential exposure and risk of Parkinson's disease that were included in the analysis

Reference	Country, period	Type of study, population, patients/controls	Exposure criterion	Disease, assessment	Risk estimate
Distance					
Huss 2009[2]	Switzerland 2000-2005	Cohort, general population	Distance from high-voltage power line	Parkinson's Mortality	0-50 m: HR=0.87 (0.50-1.56) 50-200 m: HR=1.06 (0.87-1.29) 200-600 m:HR=0.92 (0.84-1.02)
Frei 2013[4]	Denmark 1994-2011	Case-control, general population	Distance from high-voltage power line	Parkinson's Incidence	0-50 m: HR=1.14 (0.79-1.64) 50-200 m: HR=1.07 (0.92-1.25) 200-600 m: HR=0.97 (0.90-1.05)
Gervasi 2019[41]	Italy 2011-2016	Case-control, general population	Distance from high-voltage power line	Parkinson's Incidence	0-50 m: HR=1.09 (0.92-1.30) 50-200 m: HR=1.03 (0.93-1.13) 200-600 m: HR=1.00 (0.93-1.07)

Abbreviations: HR: hazard rate; OR: odds ratio.

Table 11 Studies of the association between residential exposure to magnetic fields and risk of Alzheimer's disease that were not included in the analysis

Reference	Reason for exclusion
Van der Mark 2015[55]	Use of household appliances only

6.7 Parkinson's disease and occupational exposure to magnetic fields

Table 12 Studies of the association between occupational exposure to magnetic fields and risk of Parkinson's disease that were included in the analysis

Reference	Country, period	Type of study, population, patients/controls	Exposure criterion	Disease, assessment	Risk estimate. In some cases the Committee has aggregated categories
General population					
Savitz 1998b[14]	US 1985-1991	Case-control, general population	Death certificate	Parkinson's disease, Mortality	Ever increased exposure: OR=1.1 (0.9-1.2)
Noonan 2002[15]	US 1987-1996	Case-control, general population	JEM	Parkinson's disease, Mortality	Ever increased exposure (calculated): OR=1.17 (1.00-1.38)
Feychting 2003[34]	Sweden 1981-1995	Cohort, general population	1970 occupation census, JEM	Parkinson's disease, Mortality	Ever increased exposure (calculated): RR=1.04 (0.99-1.09)
Park 2005[16]	US 1992-1998	Case-control, general population	JEM	Parkinson's disease, Mortality	Ever increased exposure: OR=0.96 (0.88-1.04)
Sorahan 2014[26]	England, Wales 1973-2010	Cohort, electricity companies	Occupational history	Parkinson's disease Mortality	Ever increased exposure (calculated): RR=1.25 (1.03-1.51)
Van der Mark 2015[55]	Netherlands 2006-2011	Case-control, general population	JEM	Parkinson's disease Incidence	Ever increased exposure (calculated): OR=0.79 (0.63-0.99)
Brouwer 2015[56]	Netherlands 1986-2003	Cohort, general population	JEM	Parkinson's disease, Mortality	Ever increased exposure (calculated): HR=1.09 (0.88-1.34)
Checkoway 2018[57]	China	Case-control, general population	JEM	Parkinson's disease, Incidence	Ever increased exposure (calculated): Prevalence ratio=1.02 (0.51-2.05)
Industrial populations					
Savitz 1998a[13]	US 1950-1986	Cohort, electricity companies	JEM	Parkinson's disease Mortality	Ever increased exposure (calculated): RR=1.10 (0.69-1.75)
Håkansson 2003[24]	Sweden 1985-1996	Cohort, engineering industry	JEM	Parkinson's disease Mortality	Ever increased exposure (calculated): RR=1.42 (0.75-2.64)
Röösli 2007[25]	Switzerland 1972-2002	Cohort, railway workers	Measure-ments, modelling	Parkinson's disease Mortality	Cumulative exposure > median: HR=0.91 (0.62-1.32)
Pedersen 2017[27]	Denmark 1982-2010	Cohort, electricity companies	JEM	Parkinson's disease Mortality	Ever increased exposure (calculated): IRR=0.68 (0.50-0.92)

Abbreviations: JEM: job-exposure matrix; HR: hazard rate; IRR: incidence rate ratio; OR: odds ratio; RR: rate ratio.

Table 13 Studies of the association between occupational exposure to magnetic fields and risk of Parkinson's disease that were not included in the analysis

Reference	Reason for exclusion
Schulte 1996[29]	No ELF exposure established a priori
Johansen 1998[32]	Update in later publication
Johansen 2000[33]	Update in later publication
Kirkey 2001[58]	No specifically exposed industries
Fryzek 2005[59]	No information on exposure
Park 2005[60]	No specifically exposed industries
Fored 2006[61]	No information on exposure
Dick 2007[62]	No specifically exposed industries
Sorahan 2007[36]	Update in later publication
Tanner 2009[63]	No information on exposure
Stampfer 2009[38]	Only specific occupations
Li 2009[64]	No specifically exposed industries
Firestone 2010[65]	No specifically exposed industries
Grell 2012[40]	Incomplete records of shocks

6.8 Multiple sclerosis (MS) and residential exposure

Table 14 Studies on the association between residential exposure and risk of MS

Reference	Country, period	Type of study, population, patients/controls	Exposure criterion	Disease, assessment	Risk estimate
Distance					
Huss 2009[2]	Switzerland 2000-2005	Cohort, general population	Distance from high-voltage power line	MS Mortality	0-50 m: HR=1.19 (0.30-4.79) 50-200 m: HR=1.45 (0.88-3.39) 200-600 m: HR=1.16 (0.89-1.51)
Frei 2013[4]	Denmark 1994-2011	Case-control, general population	Distance from high-voltage power line	MS Incidence	0-50 m: HR=1.03 (0.67-1.58) 50-<200 m: HR=1.06 (0.90-1.24) 200-<600 m: HR=1.03 (0.95-1.12)

Abbreviations: HR: hazard rate; MS: multiple sclerosis.

6.9 Multiple sclerosis (MS) and occupational exposure to magnetic fields

Table 15 Studies on the association between occupational exposure to magnetic fields and risk of MS

Reference	Country, period	Type of study, population, patients/controls	Exposure criterion	Disease, assessment	Risk estimate. In some cases the Committee has aggregated categories
General population					
Håkansson 2003[24]	Sweden 1985-1996	Cohort, engineering industry	JEM	MS Mortality	Ever increased exposure (calculated): RR=0.73 (0.40-1.34)
Industrial population					
Röösli 2007[25]	Switzerland 1972-2002	Cohort, railway workers	Measurements, modelling	MS Mortality	Cumulative exposure > median (calculated): HR=1.39 (0.23-8.38)
Pedersen 2017[27]	Denmark 1982-2010	Cohort, electricity companies	JEM	MS Mortality	Ever increased exposure: IRR=1.05 (0.64-1.74)

Abbreviations: JEM: job-exposure matrix; HR: hazard rate; IRR: incidence rate ratio; MS: multiple sclerosis; RR: rate ratio

7 Meta-analyses of the Committee

The Committee used the program RStudio, version 1.4.1106, to perform meta-analyses of the data from the available studies. Random effect analyses were used because the populations studied can differ from study to study. This chapter sets out the results of the Committee's meta-analyses.

With regard to residential exposure, sufficient data on risks is only available in relation to distance to high-voltage power lines. The Committee carried out analyses for the distance category of 0-50 m, whereby the reference distance was 400 or 600m.

In the case of occupational exposure, the main analysis compared the risks for employees who are exposed at work to a level of magnetic fields above background level and employees who are only exposed to the background level, caused by the electricity system and electrical equipment present in virtually every workplace, such as lighting, computers and household appliances. A distinction was made between studies of occupational exposure in subjects from the general population (such as case-control studies and cohort studies in the general population) and studies in subjects from specific industries, such as electricity company employees (these are usually cohort studies). Where possible, a number of subanalyses were carried out for each of these two types of study. A distinction was first made according to disease type: specific (e.g. ALS) or more general (e.g. motor neuron disease, MND). The second subanalysis relates to studies where a subject's disease was diagnosed by a physician soon after it manifested itself, compared to studies where the subject's disease was determined on the basis of information on the death certificate. In the third instance, studies in which exposure was actually measured, calculated or estimated based on a job-exposure matrix (JEM) were compared with studies in which ever practising a profession was used as the sole measure of exposure. A fourth subanalysis distinguished between studies with a complete and studies with an incomplete occupational history. Subanalyses were also carried out of highest and longest exposure, once again where possible.
The meta-analyses produce risk estimates and information on the reliability of these estimates. For further information, see the box below.

Risk estimate and confidence interval

The risk estimate shows the estimated probability of a specific effect in a specific situation relative to the control situation, in other words the relative risk. For example, a risk estimate of 1.3 means that the estimated probability of a disease occurring is 1.3 times as great, or 30% higher, in people who have been exposed than in people with no or less exposure. A risk estimate of 0.9 means that the probability found is 0.9 times as great, or 10% lower. A risk estimate of 1 means that the probability of the disease is similar in both situations.

The 95% confidence interval shows how uncertain the risk estimate is and the limits within which we expect the actual effect to lie. It means that if we were to repeat the study 100 times in the same population with different random samples, the actual effect would lie within the confidence interval in 95 cases. If the 95% confidence interval contains the value 1, we refer to the association found as not statistically significantly increased or decreased. If the lower limit of the 95% confidence interval is greater than 1, we refer to a statistically significantly increased risk. If the upper limit of the 95% confidence interval is below 1, we refer to a statistically significantly decreased risk.

7.1 Amyotrophic lateral sclerosis (ALS)

7.1.1 Distance from the residence to high-voltage power lines

The analysis shows that the risk estimate for a distance up to 50 m versus more than 400 or more than 600 m is not increased or decreased (figure 2 and table 15).

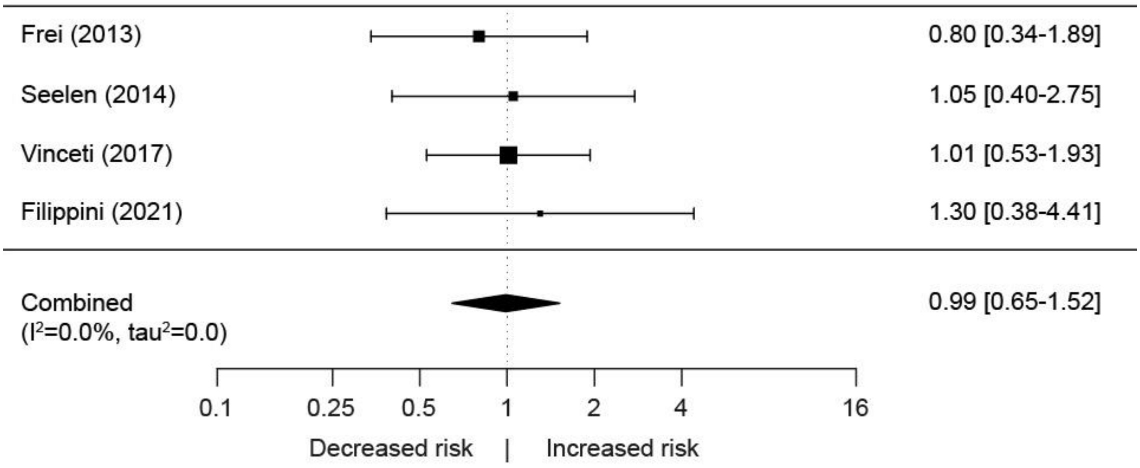


Figure 2 Meta-analysis of data on ALS and distance from the residence to high-voltage power lines. Risk estimate for 0-50 m versus >600 m.

Table 15 summarises the results of the meta-analyses.

Table 15 Analysis of data on the association between distance to a high-voltage power line and risk of ALS

Distance to high-voltage power lines (in metres)	Risk estimate	95% confidence interval	Number of studies	Heterogeneity
0-50	0.99	0.65 – 1.52	4	0.0%

7.1.2 Residential exposure to magnetic fields

Two studies were found that investigated the association between the occurrence of ALS and exposure to magnetic field strength. One study found only one ALS patient in the highest exposure group (≥0.3 µT), which means that the determination of relative risks has no significance.[3] The other study did not find any increased risks.[6] The risk estimates (with 95% confidence interval) from that study are:

- 0.1-<0.2 µT: 0.64 (0.14-2.85)
- 0.2-<0.4 µT: 1.17 (0.32-4.26)
- ≥0.4 µT: 0.27 (0.04-2.13)

7.1.3 Occupational exposure to magnetic fields

General population

For the studies in subjects from the general population, the main analysis of exposure above background levels versus background exposure shows a not statistically significantly increased risk (figure 3).

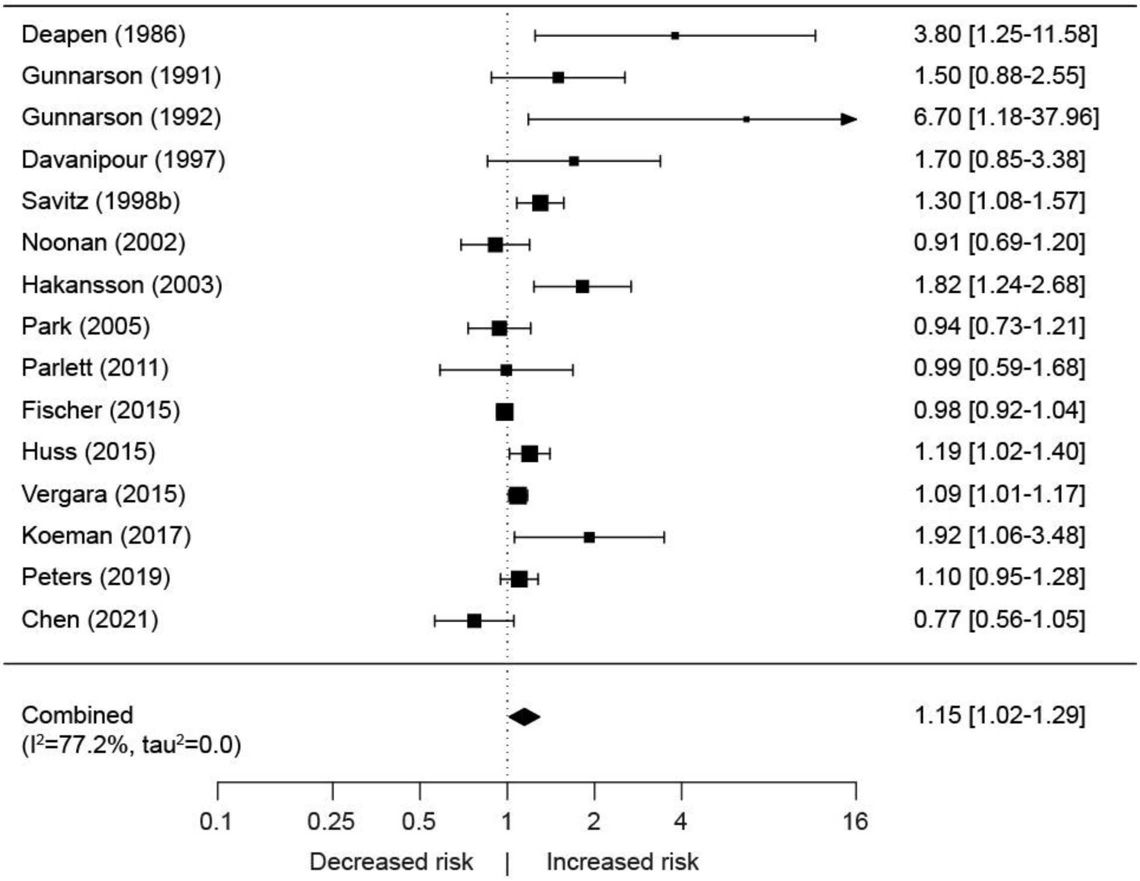


Figure 3 Meta-analysis of data on ALS and occupational exposure to magnetic fields – general population. Risk estimate from main analysis of exposure above background levels versus background exposure.

The subanalysis by disease type (ALS: specific, or MND [motor neuron disease]: more general) shows no difference in the risk estimates (p=0.07; figure 4). The risk estimate was only significantly increased for ALS.

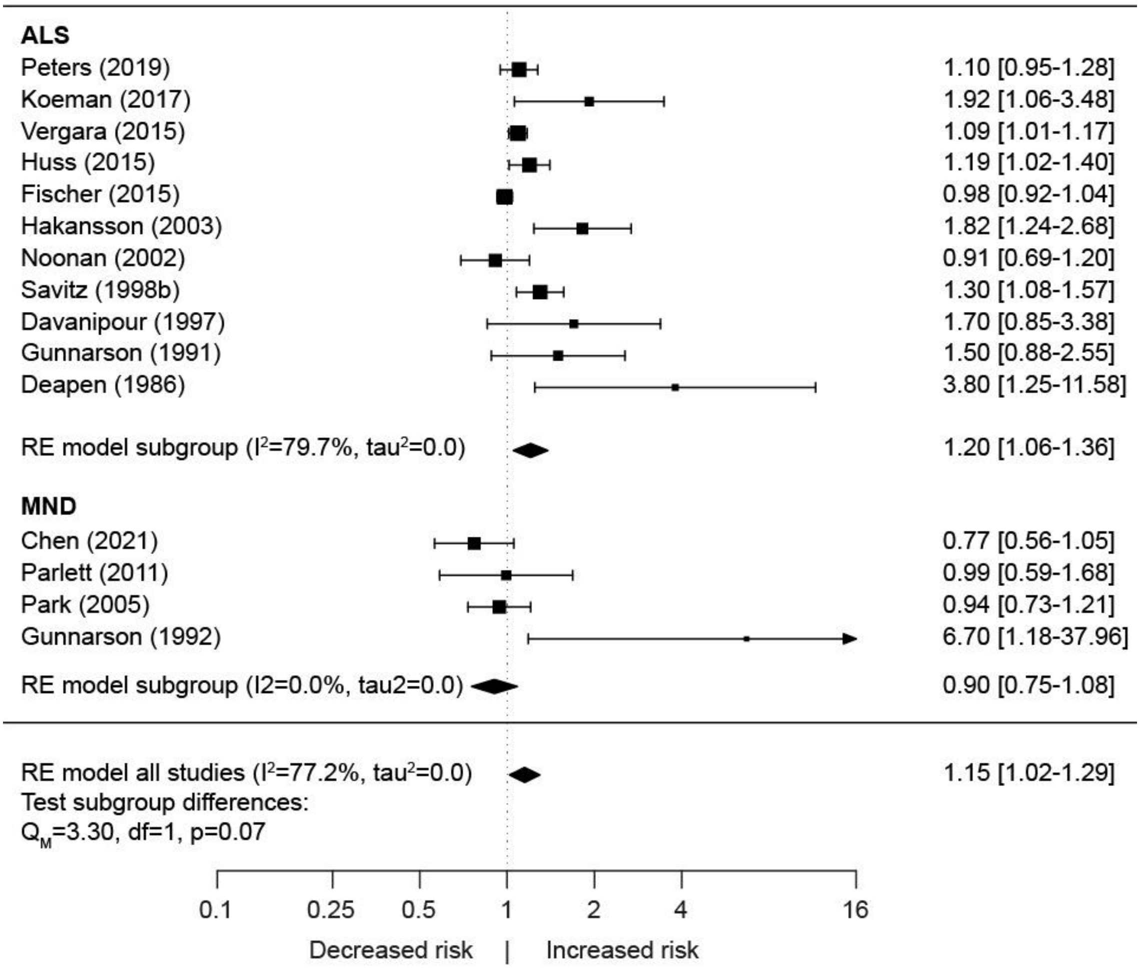


Figure 4 Meta-analysis of data on ALS and occupational exposure to magnetic fields – general population. Risk estimate from subanalysis of exposure above background levels versus background exposure for ALS or MND.

For the subanalysis according to disease detection method (diagnosis versus information from the death certificate), the risks in both categories are not statistically significantly increased, and do not differ from each other (p=0.43; figure 5).

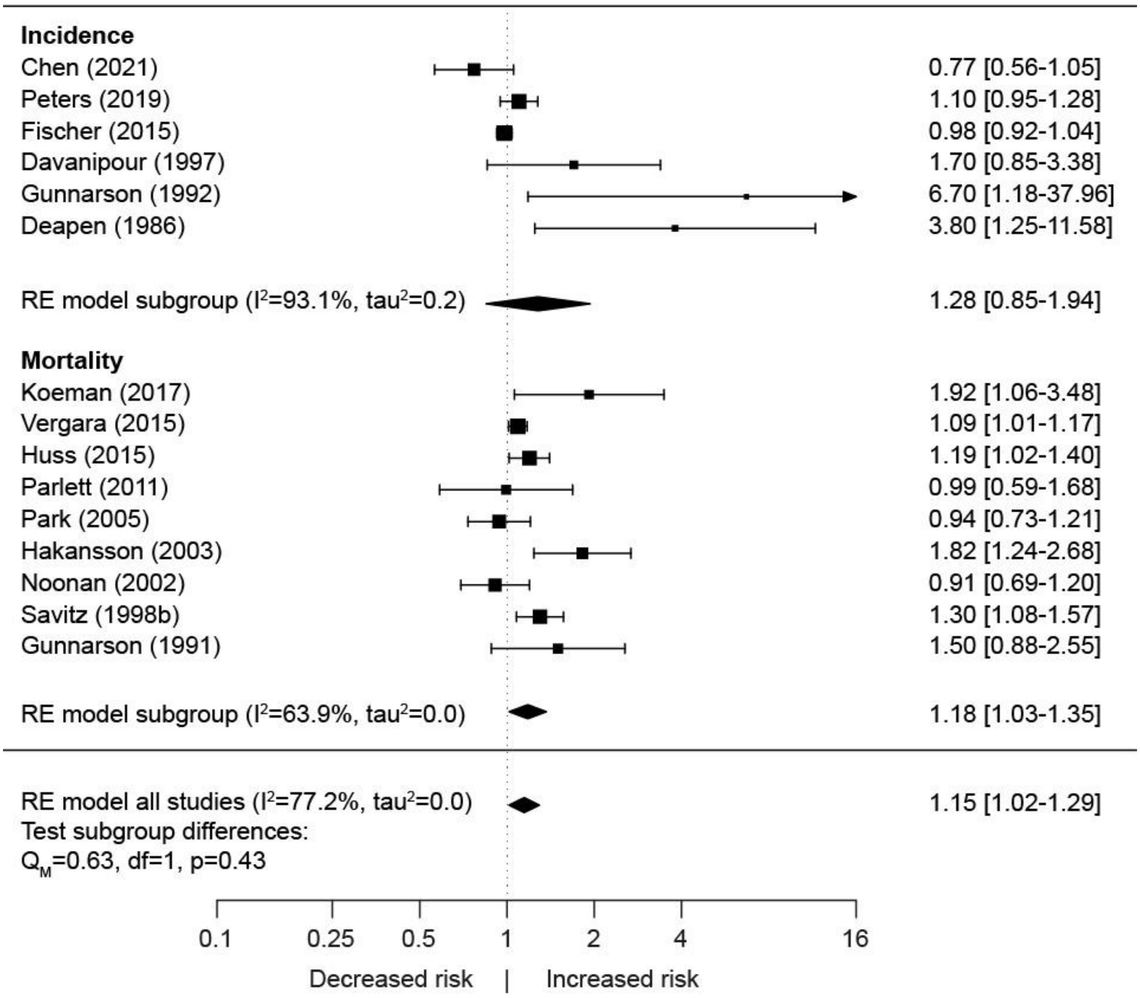


Figure 5 Meta-analysis of data on ALS and occupational exposure to magnetic fields – general population. Risk estimate from subanalysis of exposure above background levels versus background exposure for diagnosis (incidence) or information from the death certificate (mortality).

In the subanalysis according to accuracy of the exposure assessment (job-exposure matrix or actual measurements or assessment by an occupational hygienist [JEM] versus job title alone) the risk was increased in both subgroups, however this increase was only significant in the second subgroup. There was no significant difference between the two subgroups (p=0.50).

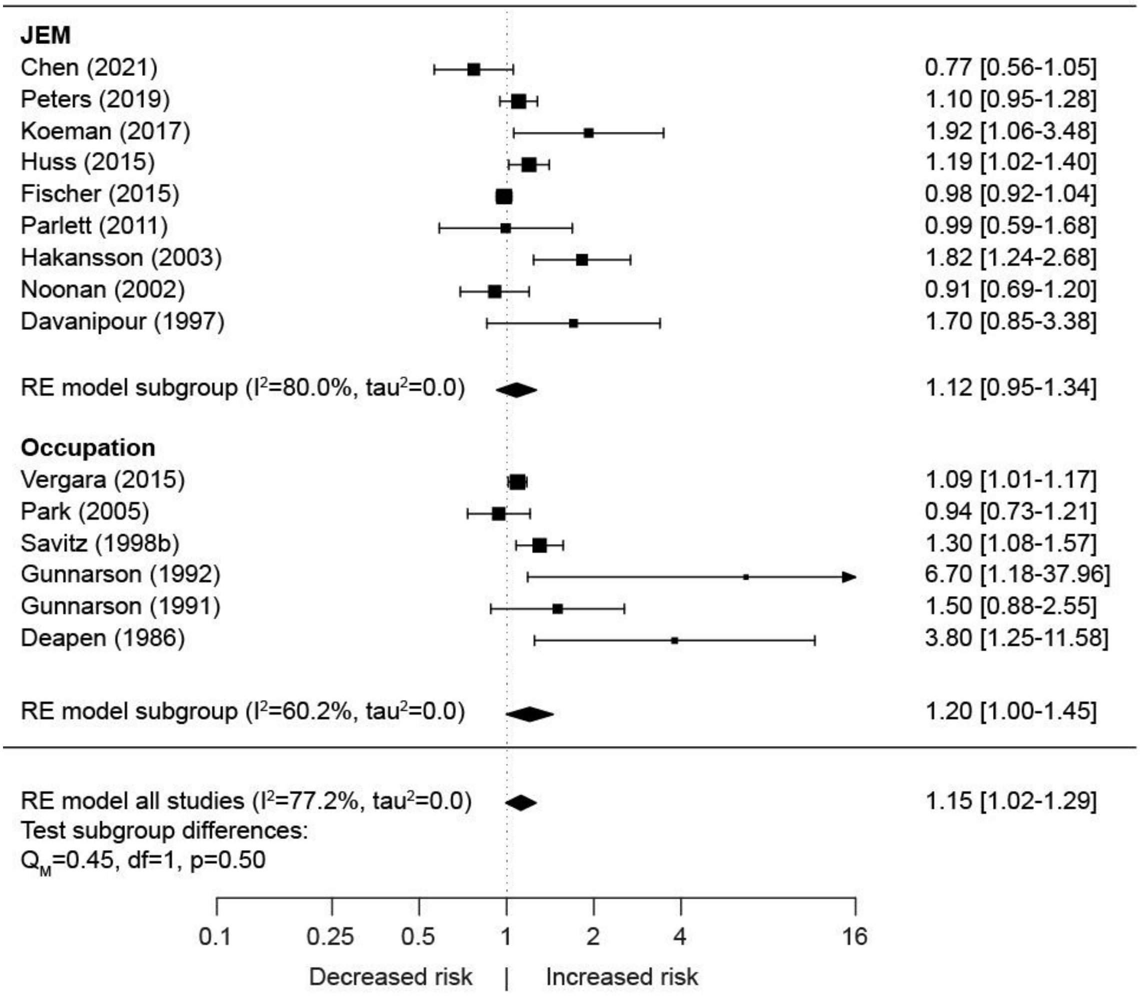


Figure 6 Meta-analysis of data on ALS and occupational exposure to magnetic fields – general population. Risk estimate from subanalysis of exposure above background levels versus background exposure for exposure as classified by a job-exposure matrix or actual measurements or assessment by an occupational hygienist (JEM) versus occupation as a proxy for exposure.

In the subanalysis according to completeness of the occupational history, the risk is not statistically significantly increased in both subgroups. The difference between the risk estimates is not significant (p=0.98; figure 7).

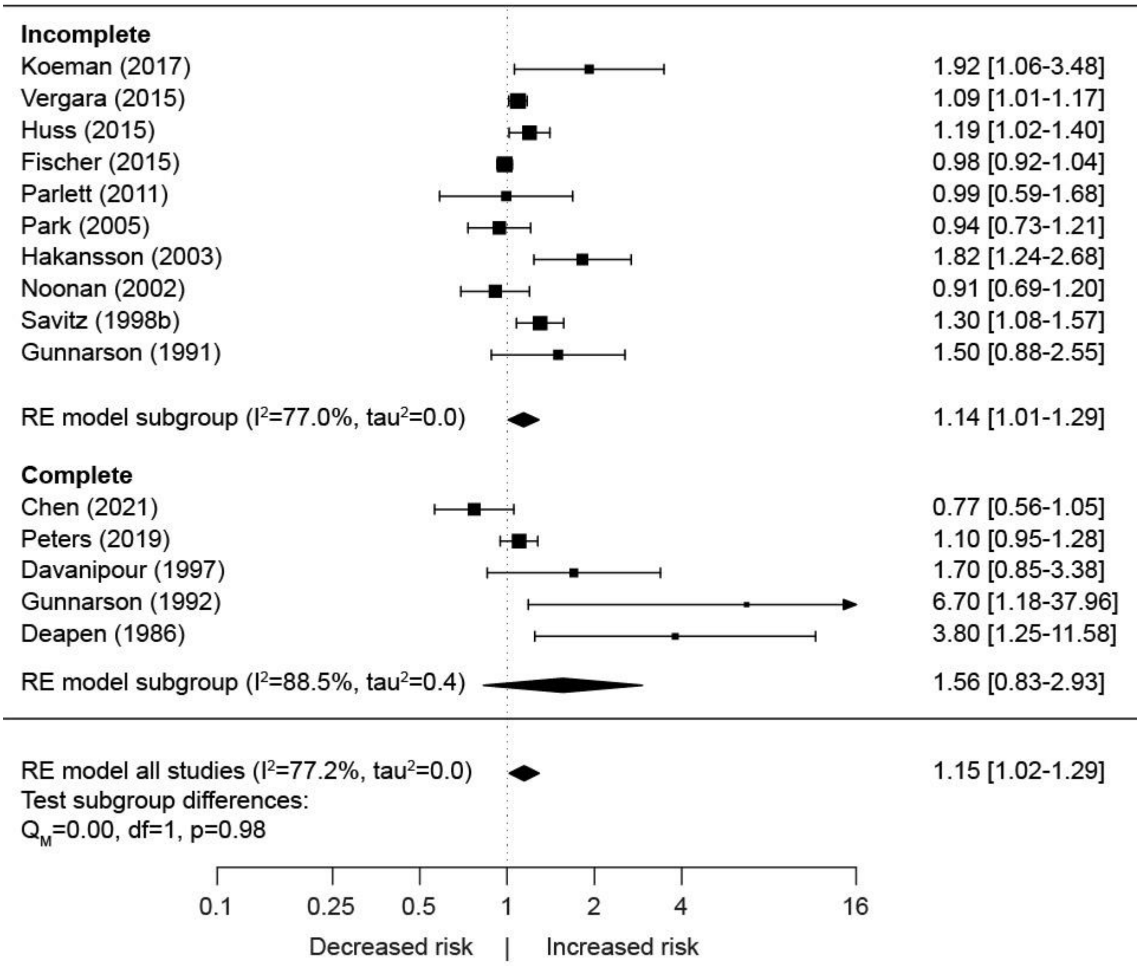


Figure 7 Meta-analysis of data on ALS and occupational exposure to magnetic fields – general population. Risk estimate from subanalysis of exposure above background levels versus background exposure for complete or incomplete occupational history.

The subanalysis of highest versus background exposure shows no increased risk (figure 8).

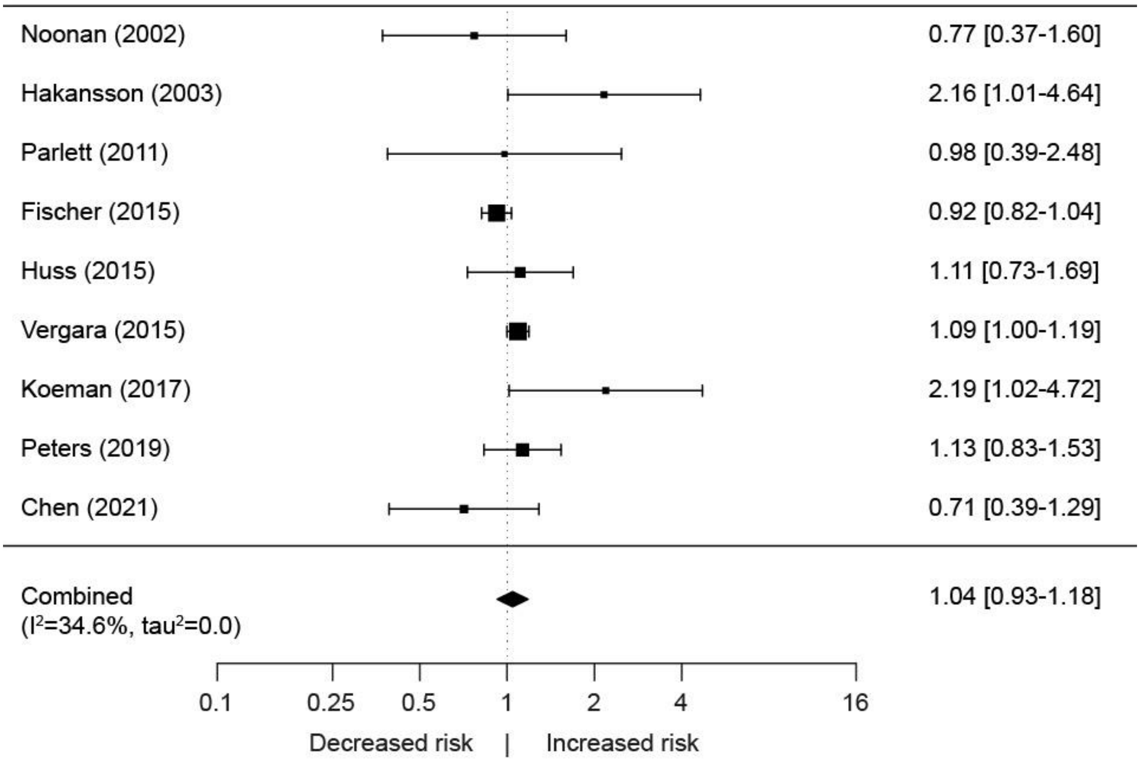


Figure 8 Meta-analysis of data on ALS and occupational exposure to magnetic fields – general population. Risk estimate from subanalysis of exposure above background levels versus background exposure.

The subanalysis of longest ever versus background exposure shows no statistically significantly increased risk (figure 9).

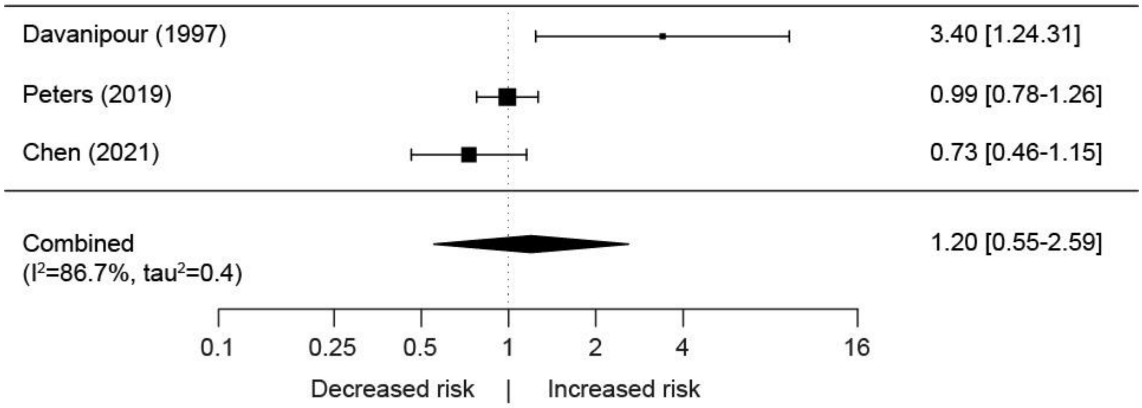


Figure 9 Meta-analysis of data on ALS and occupational exposure to magnetic fields – general population. Risk estimate from subanalysis of longest duration of exposure versus background exposure.

Industrial populations

For the studies in subjects from specific industries, the main analysis of ever versus no increased exposure shows a statistically significantly increased risk (figure 10).

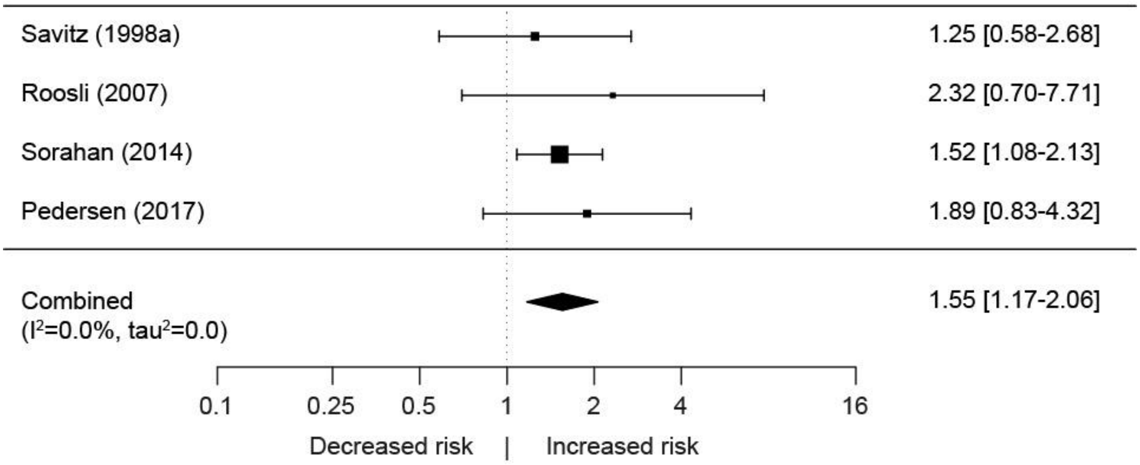


Figure 10 Meta-analysis of data on ALS and occupational exposure to magnetic fields – industrial populations. Risk estimate from main analysis of exposure above background levels versus background exposure.

Subanalyses were not possible due to the low number of studies.

Summary

Table 16 summarises the results of the meta-analyses.

Table 16 Summary of meta-analyses of data on the association between occupational exposure to magnetic fields and risk of ALS

Main analysis or subanalysis	Data analysed	Risk estimate[a]	95% confidence interval	Number of studies	Hetero-geneity	P-value difference sub-groups
Main analysis of general population	Exposure above background levels	**1.15**	**1.02 – 1.29**	15	77.2%	--
Subanalysis 1: disease	ALS	**1.20**	**1.06 – 1.36**	11	79.7%	0.07
Subanalysis 1: disease	MND	0.90	0.75 – 1.08	4	83.4%	--
Subanalysis 2: recording of disease	Incidence	1.28	0.85 – 1.94	6	93.1%	0.43
Subanalysis 2: recording of disease	Mortality	**1.18**	**1.03 – 1.35**	9	63.9%	--
Subanalysis 3: determination of exposure	Calculated/ measured	1.12	0.95 – 1.34	7	80.0%	0.50
Subanalysis 3: determination of exposure	Works in an electrical occupation	**2.63**	**1.09 – 6.32**	3	53.2%	--
Subanalysis 4: occupational history	Incomplete	**1.14**	**1.01 – 1.29**	10	77.0%	0.98
Subanalysis 4: occupational history	Complete	1.56	0.83 – 2.93	5	88.5%	--
Subanalysis 5: level of exposure	Highest exposure	1.04	0.93 – 1.18	9	34.6%	--
Subanalysis 6: duration of exposure	Longest duration of exposure	1.20	0.55 – 2.59	3	86.7%	--
Main analysis of industrial populations	Exposure above background levels	**1.55**	**1.17 – 2.06**	4	0.0%	--

[a] Statistically significant values are shown in bold.
Underlined values are included in the main report.

7.1.4 Occupational exposure to electric shocks

General population

For the studies in subjects from the general population, the main analysis of ever versus no risk of electric shocks shows a statistically significantly increased risk (figure 11).

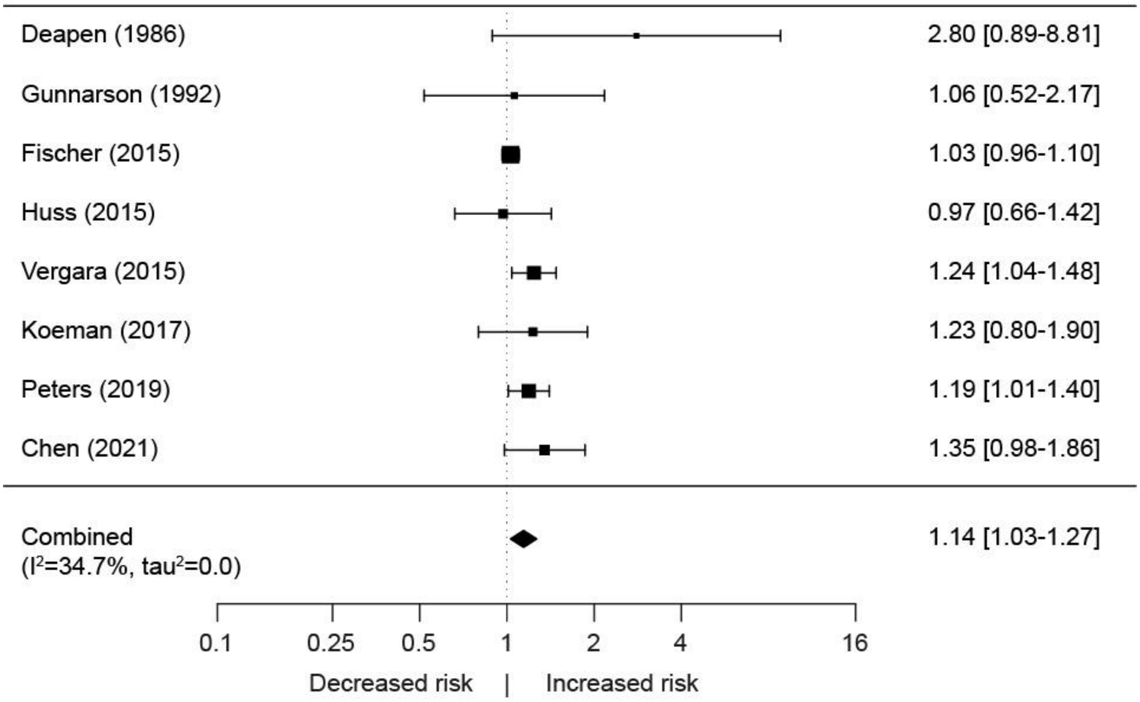


Figure 11 Meta-analysis of data on ALS and occupational exposure to electric shocks – general population. Risk estimate for main analysis of ever versus no risk of electric shocks.

The subanalysis according to disease type is only possible for specific ALS. There are only two studies of MND and it would not be useful to carry out a meta-analysis of these studies. The analysis of ALS alone shows a statistically significantly increased risk (figure 12).

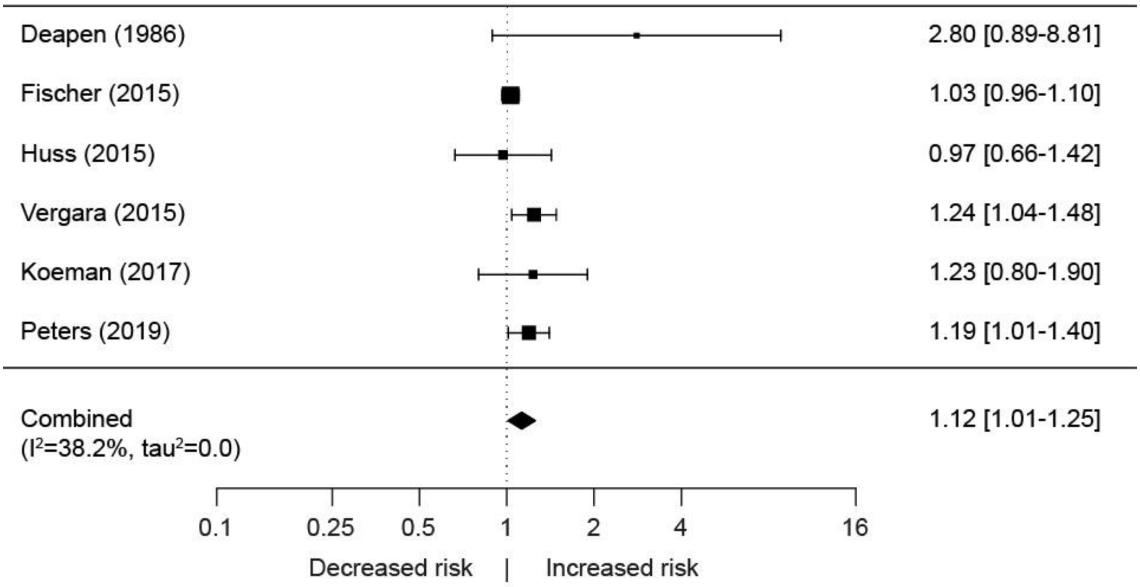


Figure 12 Meta-analysis of data on ALS and occupational exposure to electric shocks - general population. Risk estimate for subanalysis of ever versus no risk of electric shocks for ALS alone.

For the subanalysis according to disease detection method (diagnosis versus information from the death certificate), the risks in both subgroups are increased, however this increase is only statistically significant in the second subgroup (figure 13). The difference between the two subgroups is not statistically significant (p=0.74).

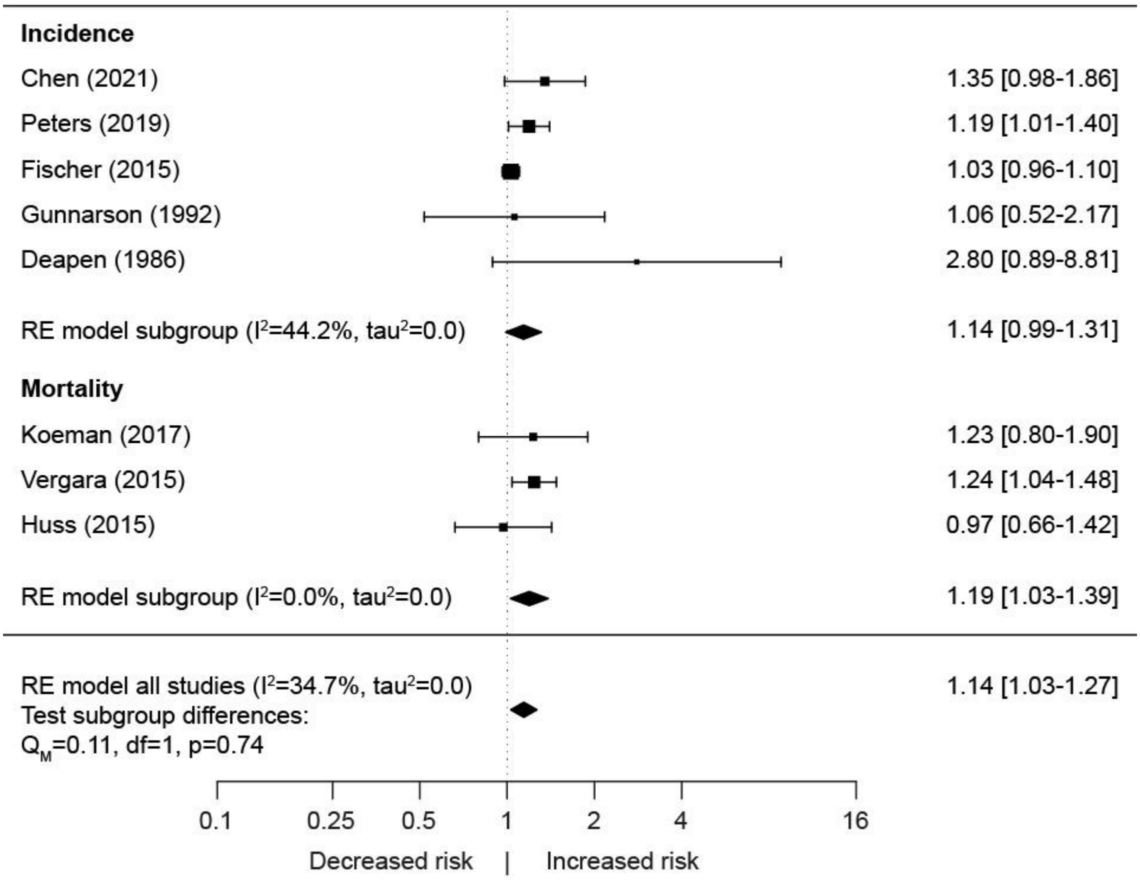


Figure 13 Meta-analysis of data on ALS and occupational exposure to electric shocks - general population. Risk estimate from subanalysis of ever versus no risk of electric shocks for diagnosis (incidence) or information from the death certificate (mortality).

In the subanalysis according to accuracy of the exposure assessment, a not statistically significantly increased risk was found for the studies in which exposure was classified by a job-exposure matrix or actual measurements or assessment by an occupational hygienist (figure 14). In the studies that used job title alone, the risk was statistically significantly increased. The difference between the two subgroups is not significant (p=0.29).

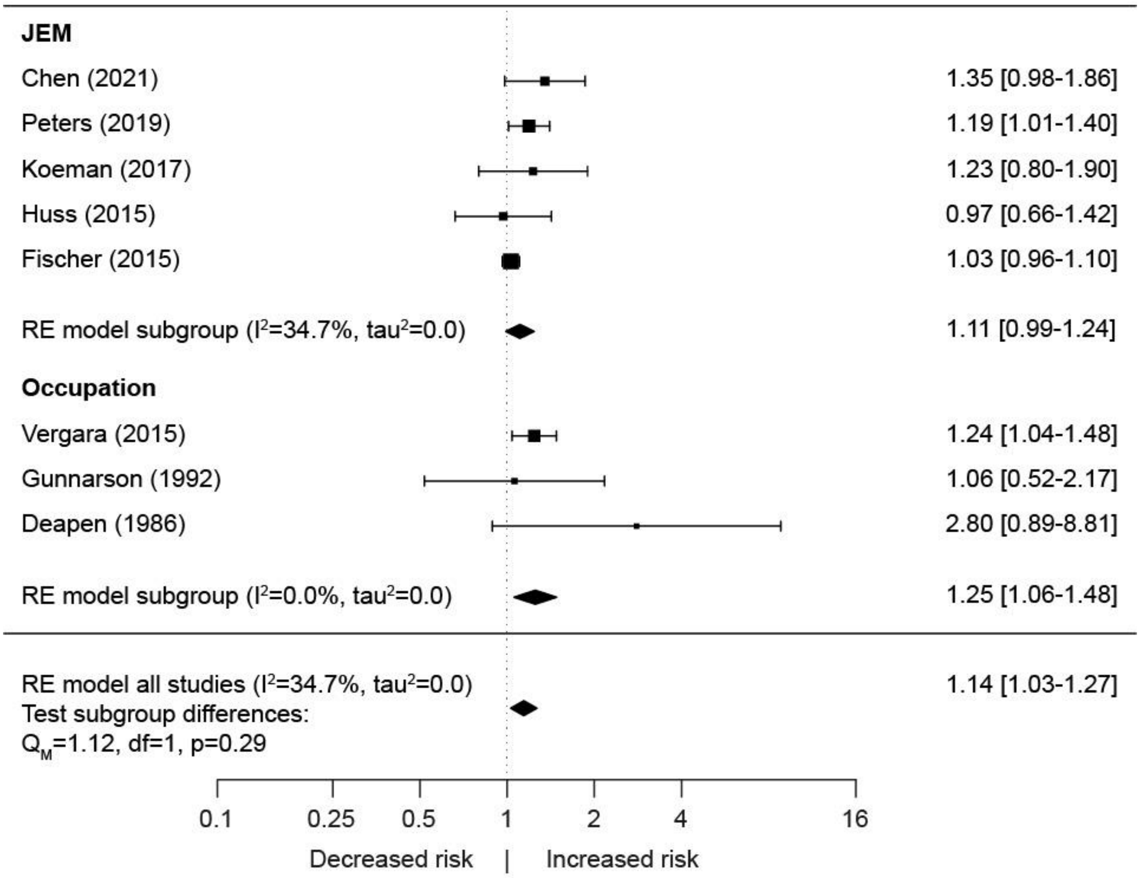


Figure 14 Meta-analysis of data on ALS and occupational exposure to electric shocks - general population. Risk estimate from subanalysis of exposure as classified by a job-exposure matrix or actual measurements or assessment by an occupational hygienist (JEM) versus occupation as a proxy for exposure.

For studies with a complete occupational history, the subanalysis shows a statistically significantly increased risk, whereas for studies with an incomplete occupational history, the risk was not statistically significantly increased (figure 15). The difference between the two groups is not significant (p=0.22).

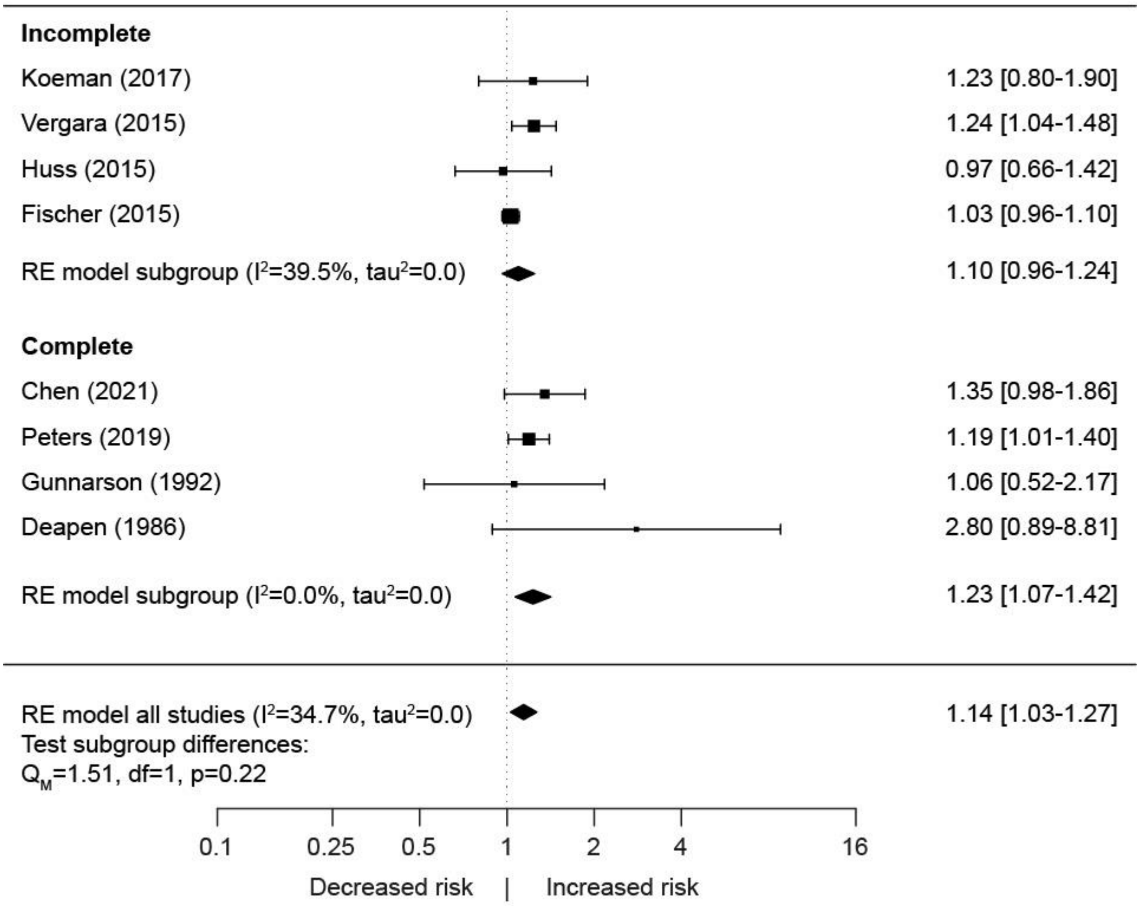


Figure 15 Meta-analysis of data on ALS and occupational exposure to electric shocks - general population. Risk estimate for subanalysis of ever versus no risk of electric shocks for complete or incomplete occupational history.

The subanalysis of highest risk of electric shocks versus no risk of electric shocks shows a not statistically significantly increased risk (figure 16).

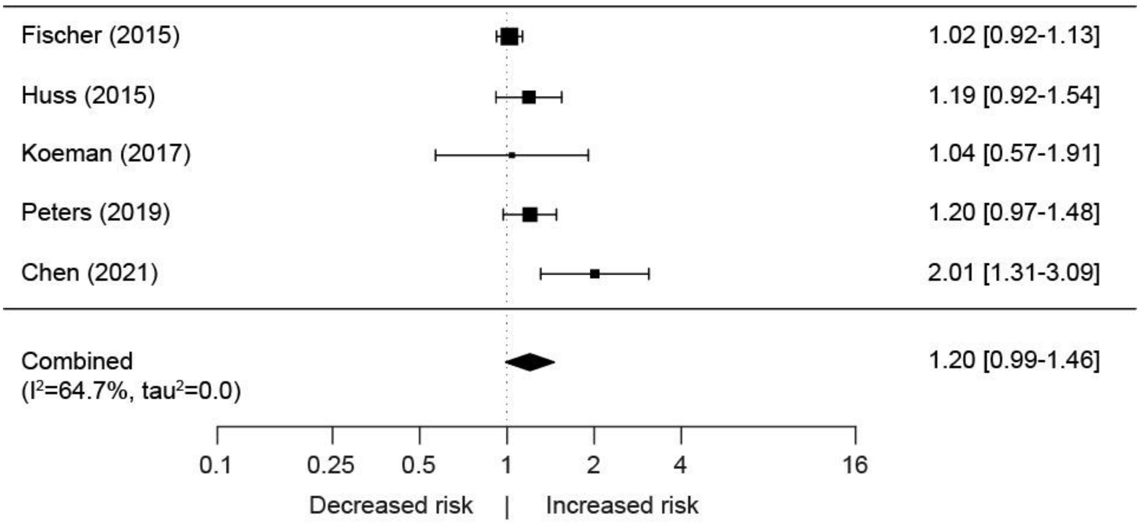


Figure 16 Meta-analysis of data on ALS and occupational exposure to electric shocks - general population. Risk estimate for subanalysis of highest risk of electric shocks versus no risk of electric shocks.

There is insufficient data for a subanalysis of longest duration of risk of electric shocks versus no risk of electric shocks.

Industrial population

There are no studies in populations from specific industries.

Summary

Table 17 summarises the results of the meta-analyses.

Table 17 Analysis of data on the association between occupational exposure to electric shocks and risk of ALS - general population.

Main analysis or subanalysis	Data analysed	Risk estimate[a]	95% confidence interval	Number of studies	Hetero-geneity	P-value difference sub-groups
Main analysis	Increased risk	**1.14**	**1.03 – 1.27**	8	34.7%	--
Subanalysis 1: disease	ALS	1.09	0.98 – 1.22	5	26.5%	--
Subanalysis 1: disease	MND	--	--	2	--	--
Subanalysis 2: recording of disease	Incidence	1.14	0.99 – 1.31	5	44.2%	0.74
Subanalysis 2: recording of disease	Mortality	**1.19**	**1.03 – 1.39**	3	0.0%	--
Subanalysis 3: determination of exposure	Calculated/ measured	1.11	0.99 – 1.24	5	34.7%	0.29
Subanalysis 3: determination of exposure	Occupation	**1.25**	**1.06 – 1.48**	3	0.0%	--
Subanalysis 4: occupation assessment	Incomplete	1.10	0.96 – 1.24	4	39.5%	0.22
Subanalysis 4: occupation assessment	Complete	**<u>1.23</u>**	**<u>1.07 – 1.42</u>**	4	0.0%	--
Subanalysis 5: level of exposure	Highest risk of shocks	1.20	0.99 – 1.46	5	64.7%	--

[a] Statistically significant values are shown in bold.
Underlined values are included in the main report.

7.1.5 Experimental studies

The Committee found three experimental studies on the association between exposure to magnetic fields and ALS. There are two studies on an animal model, which is a model for a rare familial form of ALS.[66,67] There is also one study on a model involving cultured cells.[68] None of these studies showed effects at exposures up to 1 mT (approximately a factor of 100-1000 higher than residential or occupational exposures).

7.2 Alzheimer's disease

7.2.1 Distance from home to high-voltage power lines

The analysis showed no association between distance to high-voltage power lines and risk of Alzheimer's disease. The risk estimate for a distance of 0 to 50 m versus more than 600 m is not statistically significantly increased (see figure 17).

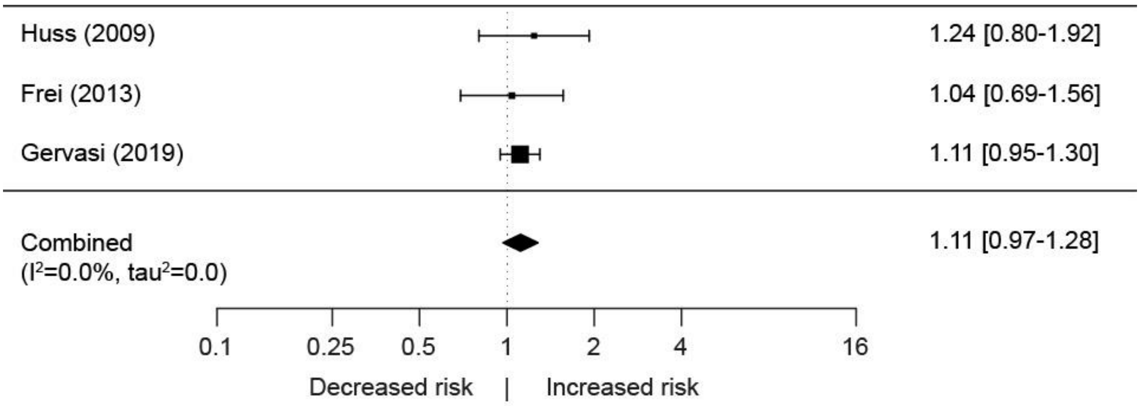


Figure 17 Meta-analysis of data on Alzheimer's disease and distance from home to high-voltage power lines. Risk estimate for 0-50 m versus >600 m.

Table 18 summarises the results of the meta-analyses.

Table 18 Analysis of data on the association between distance to a high-voltage power line and risk of Alzheimer's disease

Distance to high-voltage power lines (in metres)	Risk estimate	95% confidence interval	Number of studies	Heterogeneity
0-50	1.11	0.97-1.28	3	0.0%

7.2.2 Residential exposure to magnetic fields

There are no studies that determine residential exposure to magnetic fields.

7.2.3 Occupational exposure to magnetic fields

General population

For the studies in subjects from the general population, the main analysis of exposure above background levels versus background exposure show a statistically significantly increased risk (figure 18).

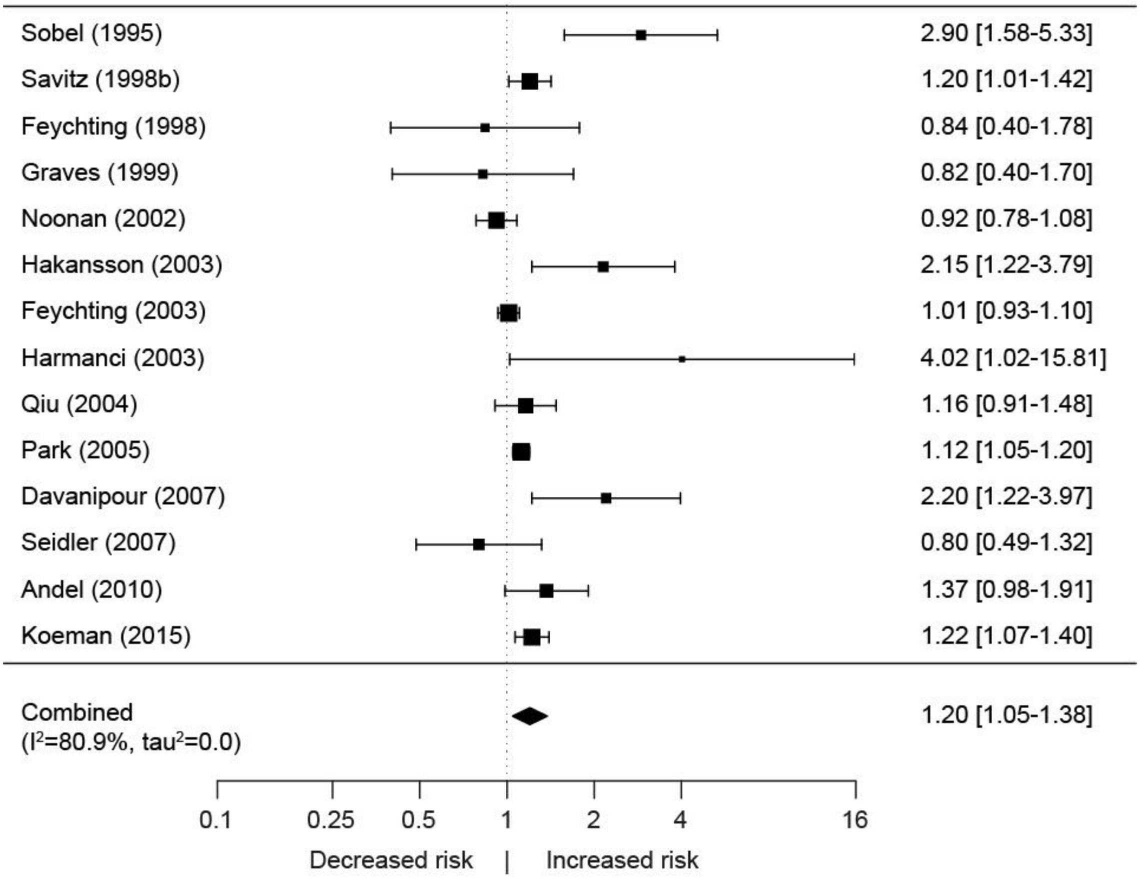


Figure 18 Meta-analysis of data on Alzheimer's disease and occupational exposure to magnetic fields - general population. Risk estimate from main analysis of exposure above background levels versus background exposure.

The subanalysis according to disease type (Alzheimer's: specific, or non-vascular dementia: more general) is only possible for Alzheimer's, as there is only one study of non-vascular dementia. The analysis of Alzheimer's disease alone shows a statistically significantly increased risk (figure 19).

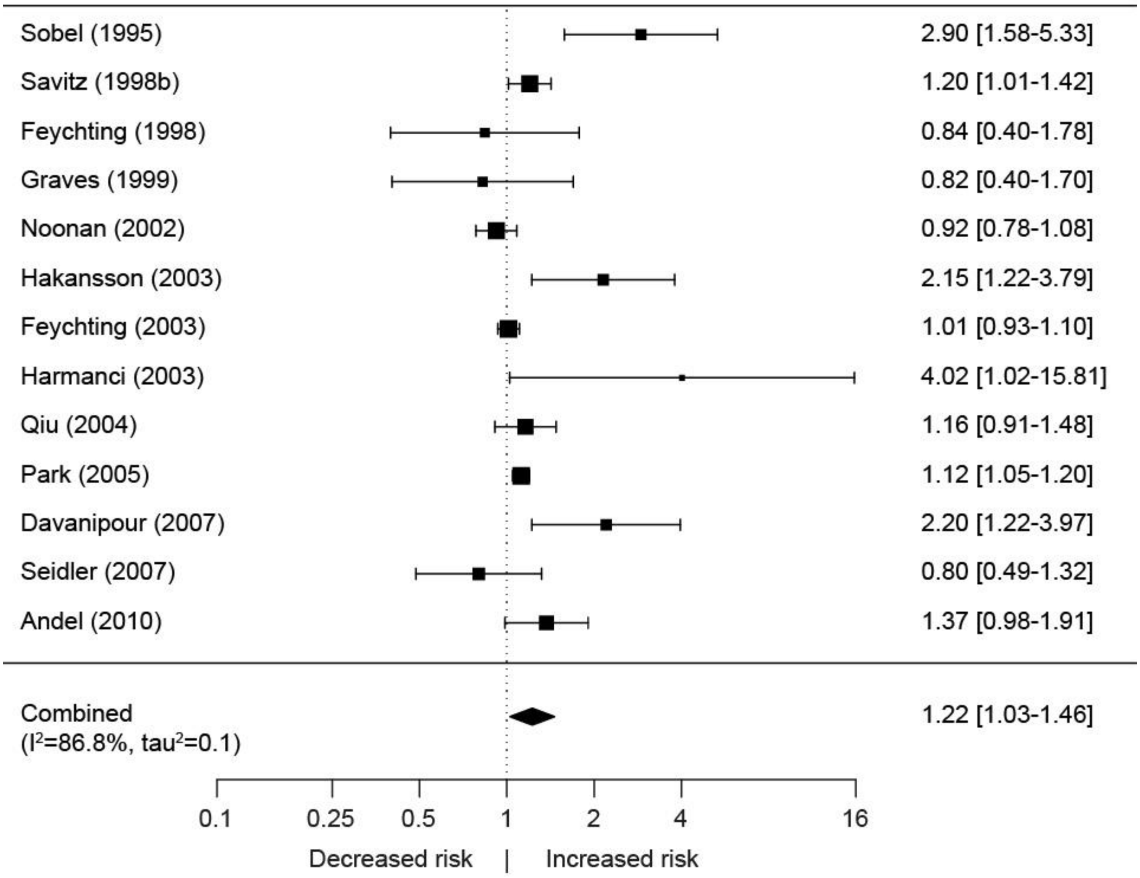


Figure 19 Meta-analysis of data on Alzheimer's disease and occupational exposure to magnetic fields - general population. Risk estimate from subanalysis of exposure above background levels versus background exposure for Alzheimer's disease alone.

For the subanalysis according to disease detection method (diagnosis versus information from the death certificate), the risks in both categories are increased, however this increase is only statistically significant in the second subcategory. The difference between the two subgroups is not significant (p= 0.29; figure 20).

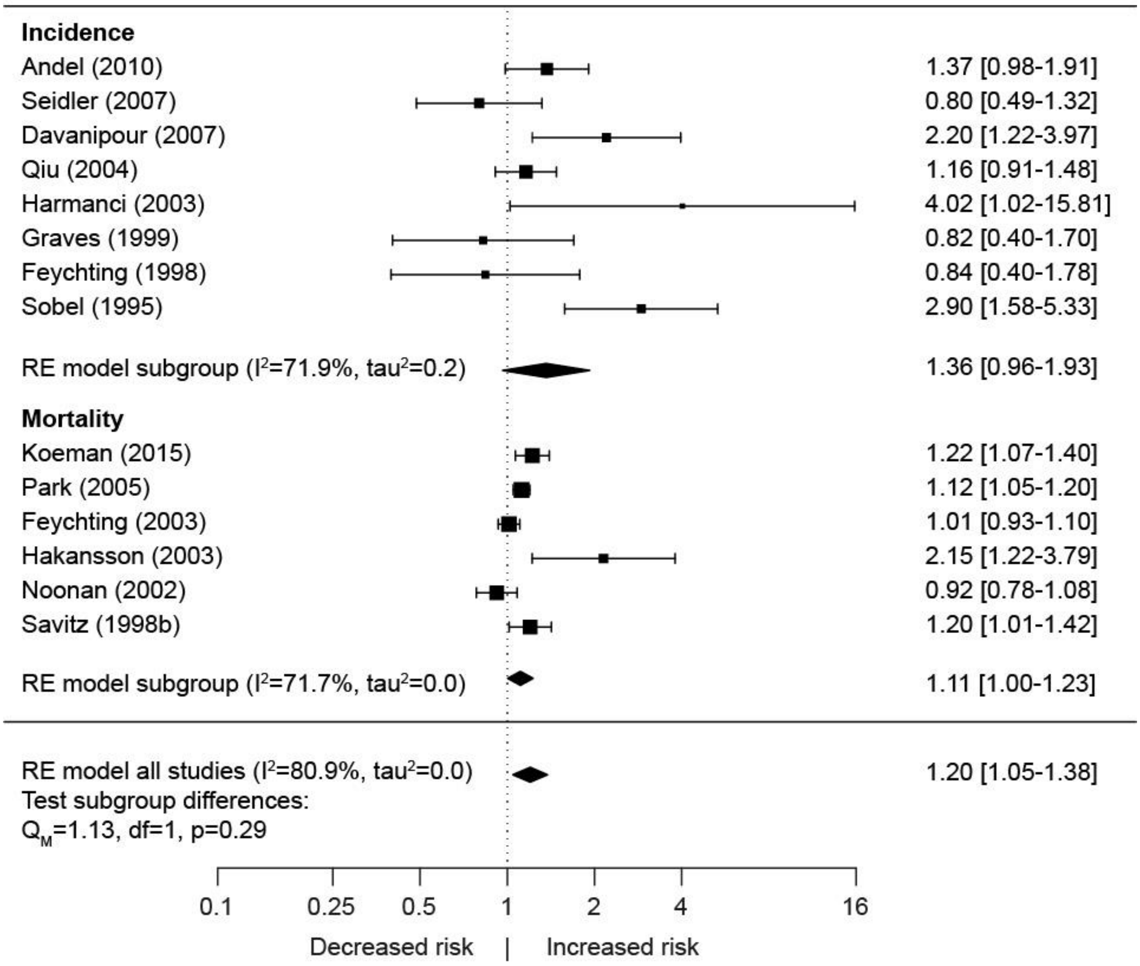


Figure 20 Meta-analysis of data on Alzheimer's disease and occupational exposure to magnetic fields - general population. Risk estimate from subanalysis of exposure above background levels versus background exposure for diagnosis or information from the death certificate.

A subanalysis according to accuracy of the exposure assessment could only be carried out on the studies that used a job-exposure matrix or actual measurements or assessment by an occupational hygienist. There are only two studies that used job title alone. The risk in the first subcategory was statistically significantly increased (figure 21).

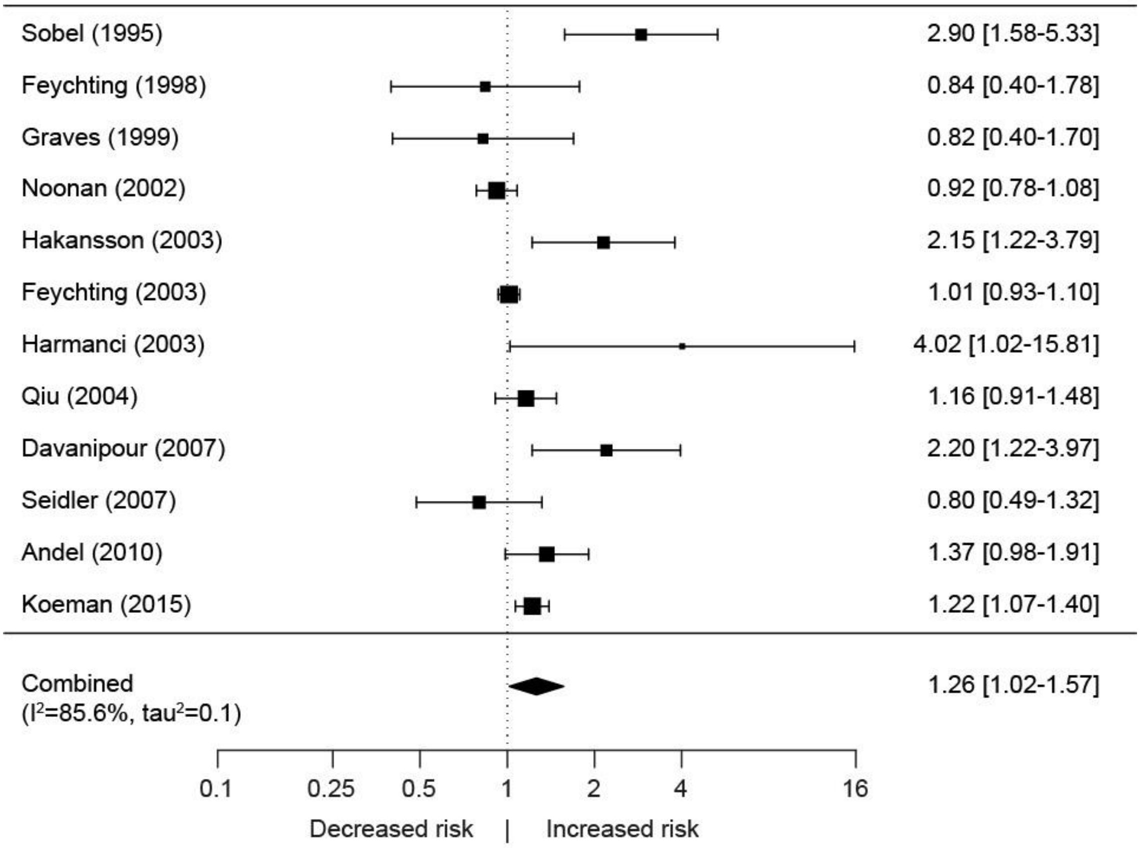


Figure 21 Meta-analysis of data on Alzheimer's disease and occupational exposure to magnetic fields - general population. Risk estimate for subanalysis of exposure above background levels versus background exposure for studies that used a job-exposure matrix or actual measurements or assessment by an occupational hygienist.

The risk was statistically significantly increased for both studies with a complete and an incomplete occupational history (figure 22). The difference between the two subgroups is not significant (p=0.15).

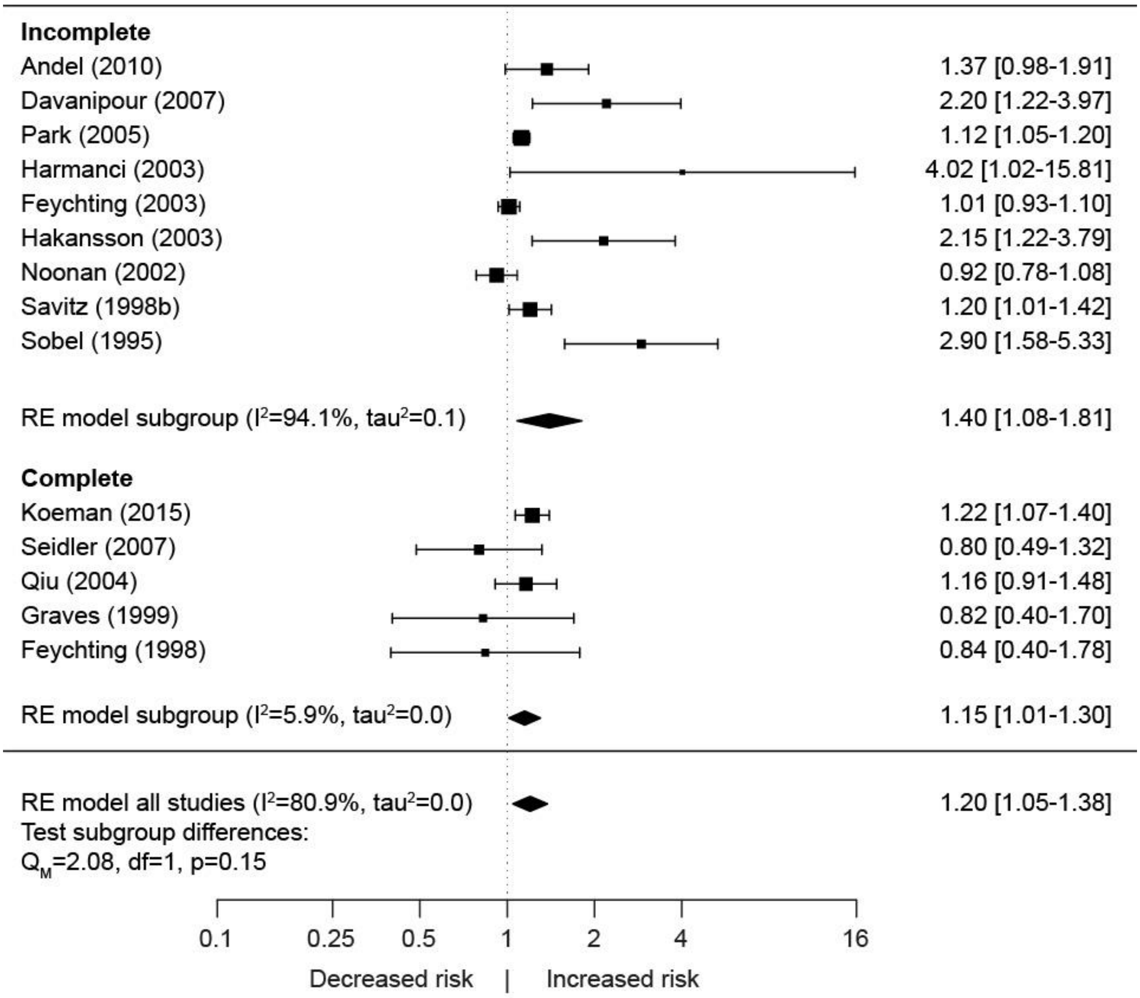


Figure 22 Meta-analysis of data on Alzheimer's disease and occupational exposure to magnetic fields - general population. Risk estimate from subanalysis of exposure above background levels versus background exposure for complete or incomplete occupational history.

The subanalysis of highest versus not exposed shows a statistically significantly increased risk (figure 23).

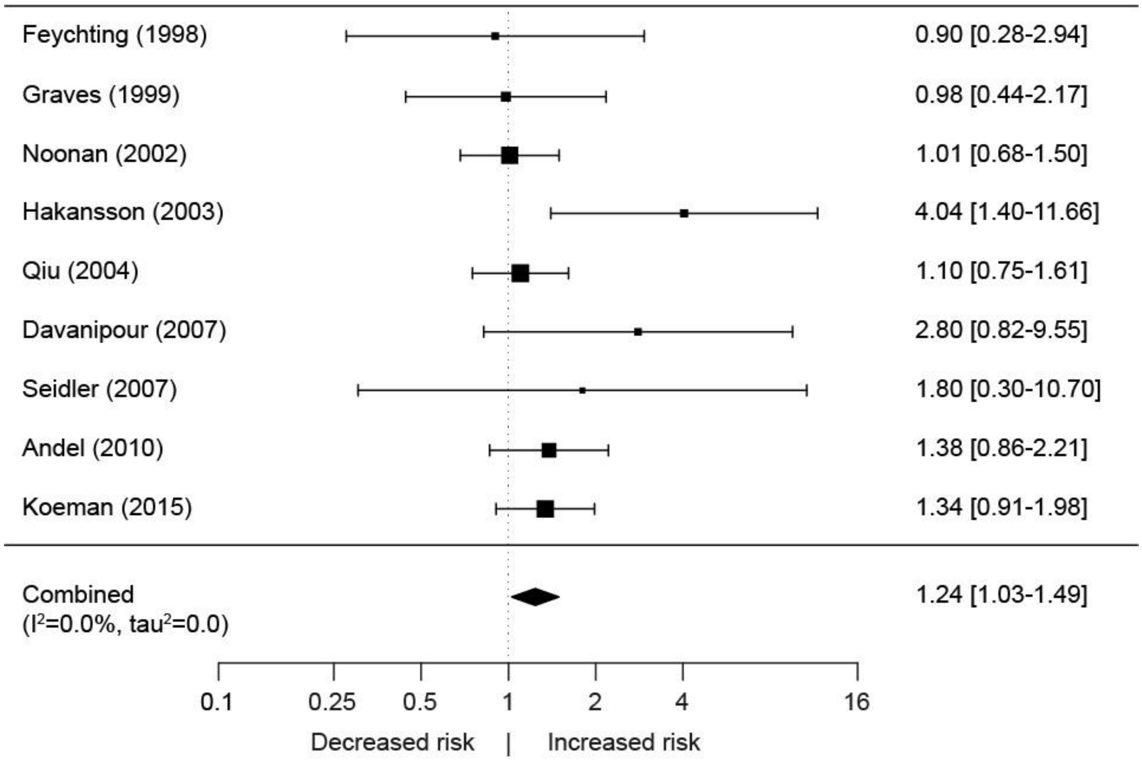


Figure 23 Meta-analysis of data on Alzheimer’s disease and occupational exposure to magnetic fields - general population. Risk estimate from subanalysis of exposure above background levels versus background exposure.

There is no data on longest duration of increased exposure versus not increased exposure.

Industrial populations

For the studies in subjects from specific industries, the main analysis of exposure above background levels versus background exposure shows a not statistically significant increased risk (see figure 24).

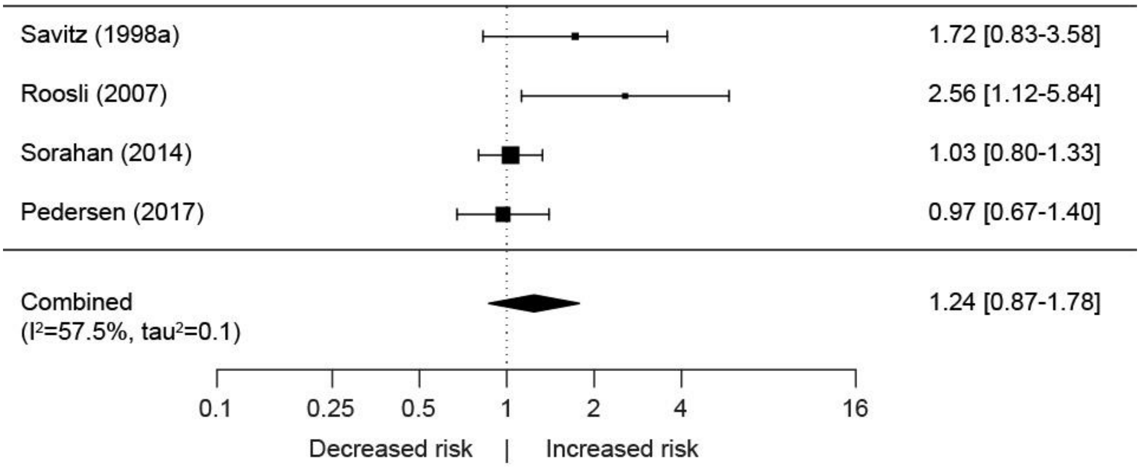


Figure 24 Meta-analysis of data on Alzheimer's disease and occupational exposure to magnetic fields – industrial populations. Risk estimate from main analysis of exposure above background levels versus background exposure.

Due to the low number of studies in subjects from specific industries, subanalyses were not possible. Neither is there sufficient data for an analysis of highest or longest exposure above background levels versus background exposure.

Summary

Table 19 summarises the results of the meta-analyses.

Table 19 Analysis of data on the association between occupational exposure to magnetic fields and risk of Alzheimer's disease

Main analysis or subanalysis	Data analysed	Risk estimate[a]	95% confidence interval	Number of studies	Hetero-geneity	P-value difference sub-groups
Main analysis of general population	Exposure above background levels	**1.20**	**1.05 – 1.38**	14	80.9%	--
Subanalysis 1: disease	Alzheimer's disease	**1.22**	**1.03 – 1.46**	13	86.8%	--
Subanalysis 1: disease	Non-vascular dementia	--	--	1	--	--
Subanalysis 2: recording of disease	Incidence	1.36	0.96 – 1.93	8	71.9%	0.29
Subanalysis 2: recording of disease	Mortality	**1.11**	**1.00 – 1.23**	6	71.7%	--
Subanalysis 3:	Calculated/ measured	**1.26**	**1.02 – 1.57**	12	85.6%	--
Subanalysis 3:	Occupation	--	--	--	--	--
Subanalysis 4: occupational history	Incomplete	**1.40**	**1.08 – 1.81**	8	94.1%	0.15
Subanalysis 4: occupational history	Complete	**1.15**	**1.01 – 1.30**	5	5.9%	--
Subanalysis 5: level of exposure	Highest exposure	**1.24**	**1.03 – 1.49**	9	0.0%	--
Main analysis of industrial populations	Exposure above background levels	1.24	0.87 – 1.78	4	57.5%	--

[a] Statistically significant values are shown in bold.
Underlined values are included in the main report.

7.2.4 Experimental studies

In five studies on animal models for Alzheimer's disease, exposure to magnetic fields was found to have health benefits in the form of improvements in cognitive ability of the animals showing Alzheimer's characteristics.[66,69-72] Two other studies found no negative health effects in healthy animals.[73,74] The exposure levels varied from 100 µT to 10 mT.

Six studies were also found on cellular models for Alzheimer's disease (i.e. studies of cultured cells). Two found no effects of exposure to magnetic fields[75,76], three found effects that may indicate pathological effects[77-79] and one study found a potentially beneficial effect.[80] The exposure levels ranged from 50 µT to 3.1 mT.

7.3 Parkinson's disease

7.3.1 Distance from the residence to high-voltage power lines

The analysis shows no association between distance to high-voltage power lines and risk of Parkinson's disease. The risk estimate for a distance of 0 to 50 m versus more than 600 m is not statistically significantly increased (see figure 25).

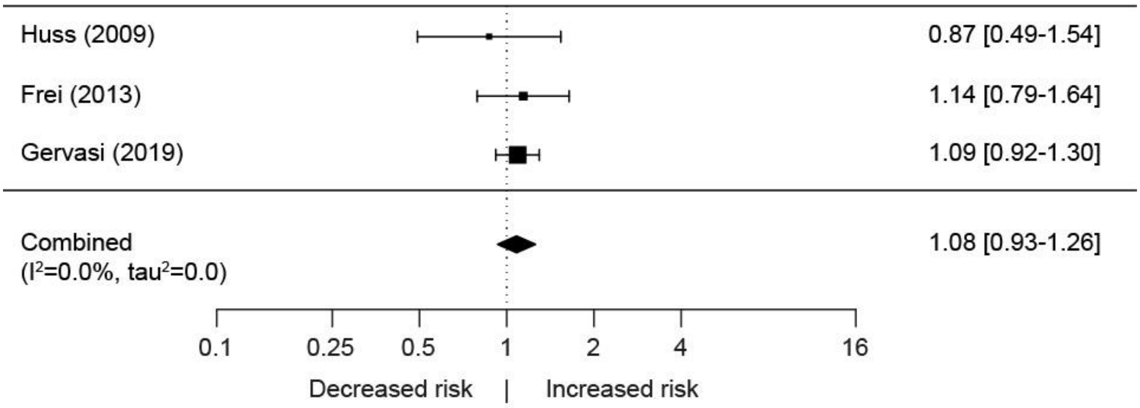


Figure 25 Meta-analysis of data on Parkinson's disease and distance from the residence to high-voltage power lines. Risk estimate for 0-50 m versus >600 m.

Table 20 summarises the results of the meta-analyses.

Table 20. Analysis of data on the association between distance to a high-voltage power line and risk of Parkinson's disease

Distance to high-voltage power lines (in metres)	Risk estimate	95% confidence interval	Number of studies	Heterogeneity
0-50 [b]	1.08	0.93-1.26	3	0.0%

7.3.2 Residential exposure to magnetic fields

There are no studies that assess residential exposure to magnetic fields.

7.3.3 Occupational exposure to magnetic fields

General population

The main analysis of occupational exposure above background levels versus background exposure for studies in subjects from the general population shows no increased risk (figure 26).

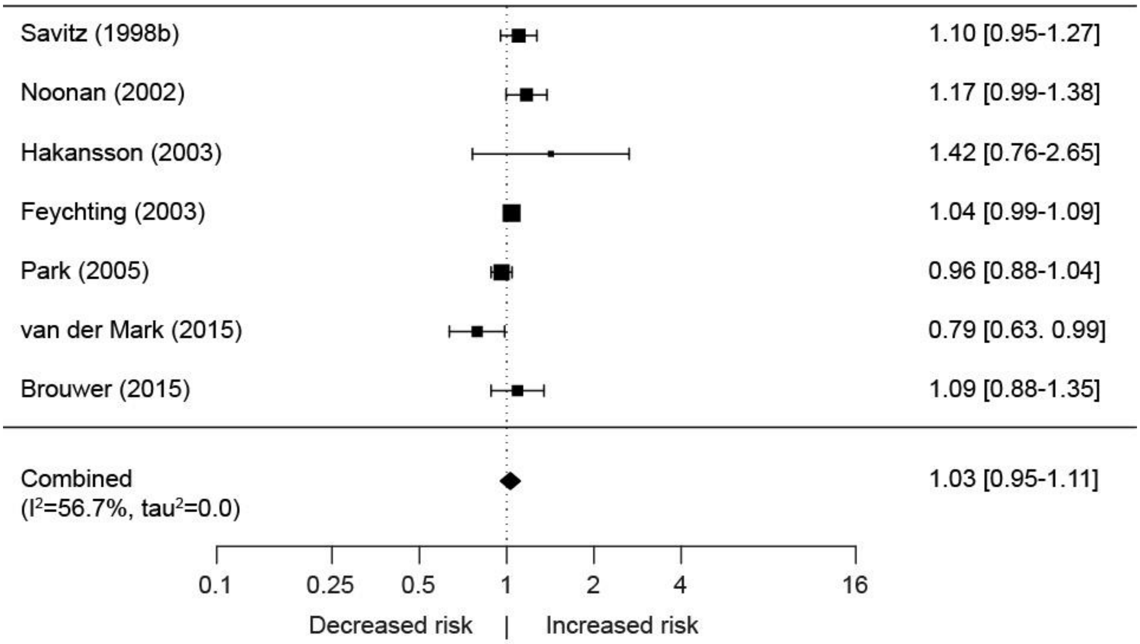


Figure 26 Meta-analysis of data on Parkinson's disease and occupational exposure to magnetic fields - general population. Risk estimate from main analysis of exposure above background levels versus background exposure.

The subanalysis according to disease type (Parkinson's: specific or Parkinson's as primary and secondary cause of death: more general) is only possible for Parkinson's, as there is only one study of Parkinson's disease as primary and secondary cause of death. The analyses of the Parkinson's studies show no increased risk (figure 27).

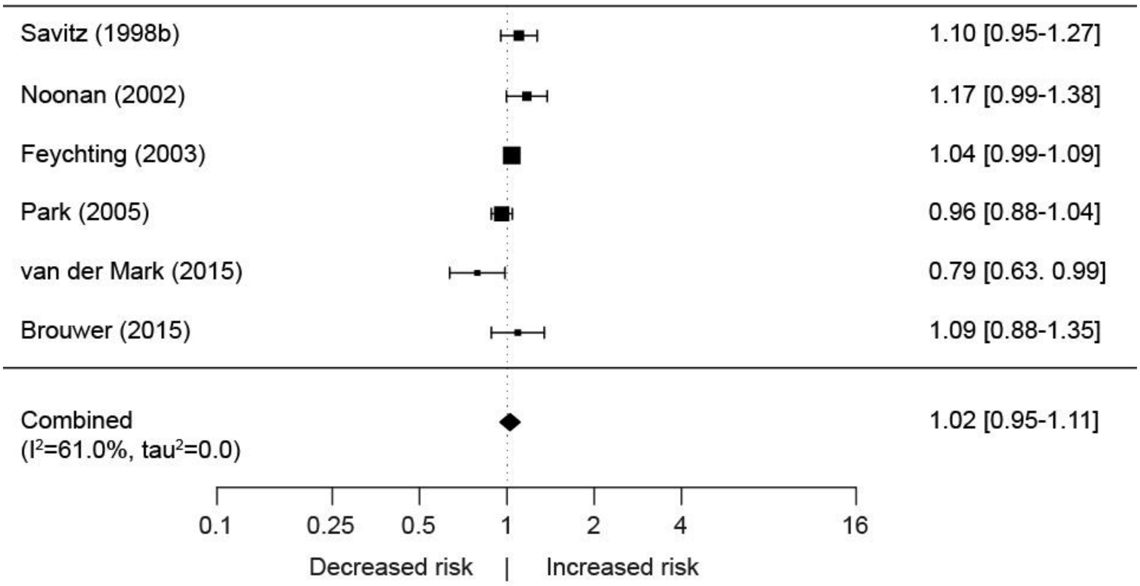


Figure 27 Meta-analysis of data on Parkinson's disease and occupational exposure to magnetic fields - general population. Risk estimate from subanalysis of exposure above background levels versus background exposure for Parkinson's disease alone.

The subanalysis according to disease detection method (diagnosis versus information from the death certificate) is only possible for the studies with information from the death certificate, as there is only one study using diagnosis. The analysis of the studies using information from the death certificate shows no increased risk (figure 28).

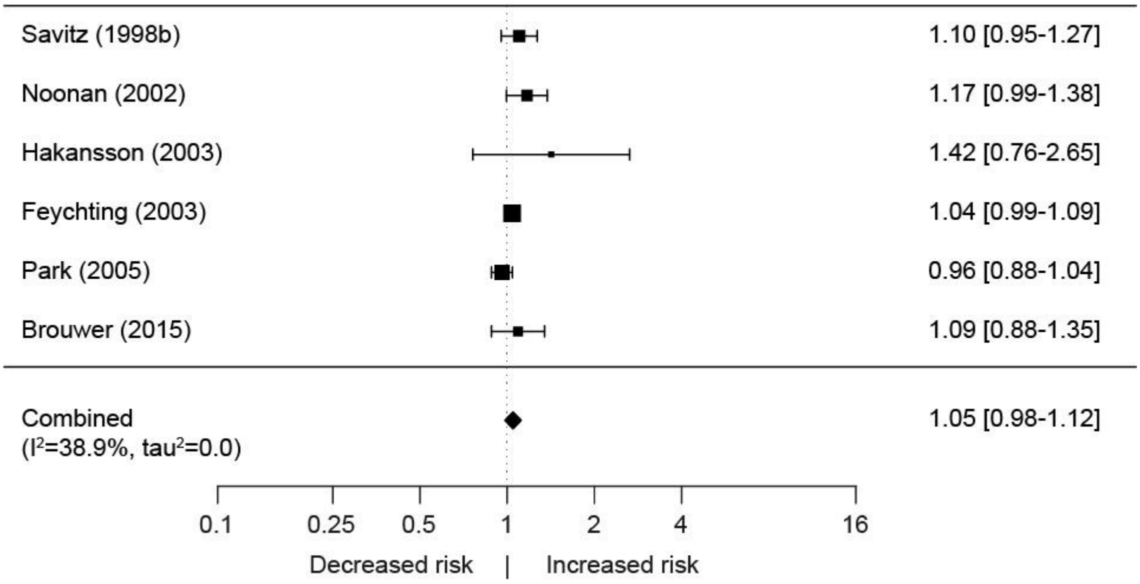


Figure 28 Meta-analysis of data on Parkinson’s disease and occupational exposure to magnetic fields - general population. Risk estimate from subanalysis of exposure above background levels versus background exposure for information from the death certificate alone.

A subanalysis according to accuracy of the exposure assessment could only be carried out on the studies that used a job-exposure matrix or actual measurements or assessment by an occupational hygienist. There are only two studies that used job title alone. The analysis shows no increased risk (figure 29).

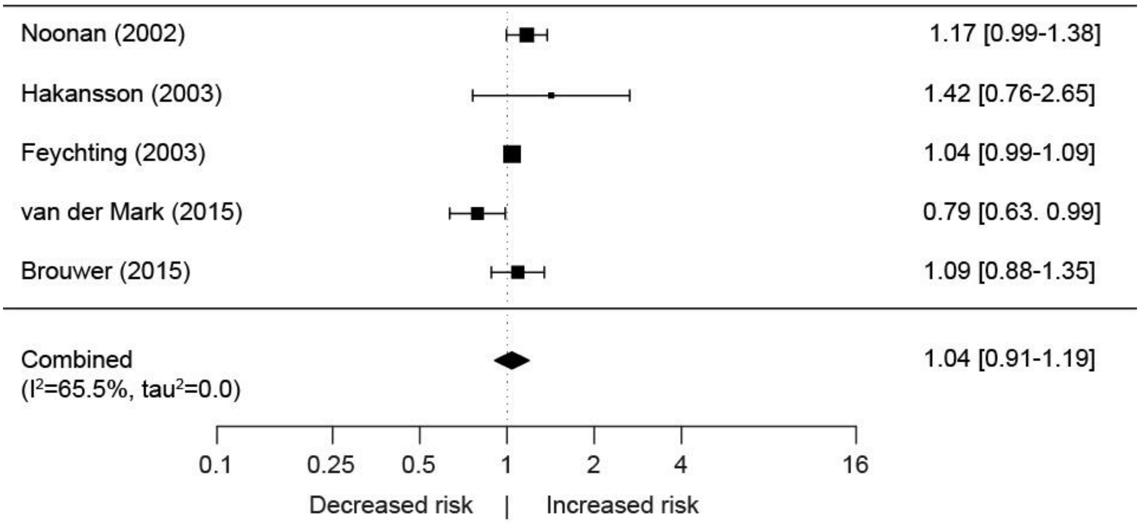


Figure 29 Meta-analysis of data on Parkinson's disease and occupational exposure to magnetic fields - general population. Risk estimate for subanalysis of exposure above background levels versus background exposure for studies in which exposure was classified by a job-exposure matrix or actual measurements or assessment by an occupational hygienist.

A subanalysis according to completeness of occupational history could only be carried out on the studies involving an incomplete occupational history, as there are only two studies involving a complete occupational history. The analysis shows no increased risk (figure 30).

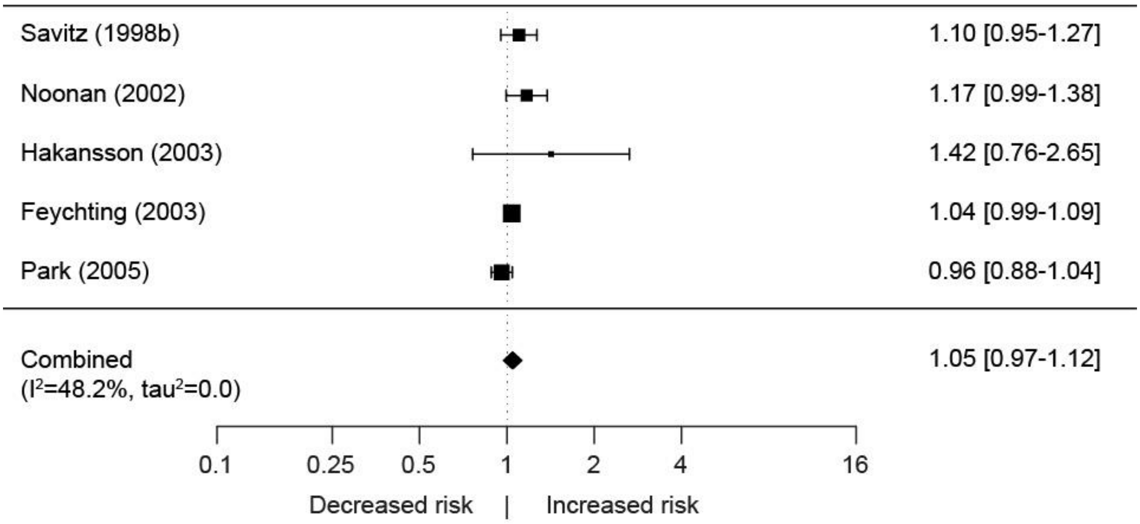


Figure 30 Meta-analysis of data on Parkinson's disease and occupational exposure to magnetic fields - general population. Risk estimate from subanalysis of exposure above background levels versus background exposure for studies involving an incomplete occupational history.

The subanalysis of the highest exposure above background levels versus background exposure shows no increased risk (figure 31).

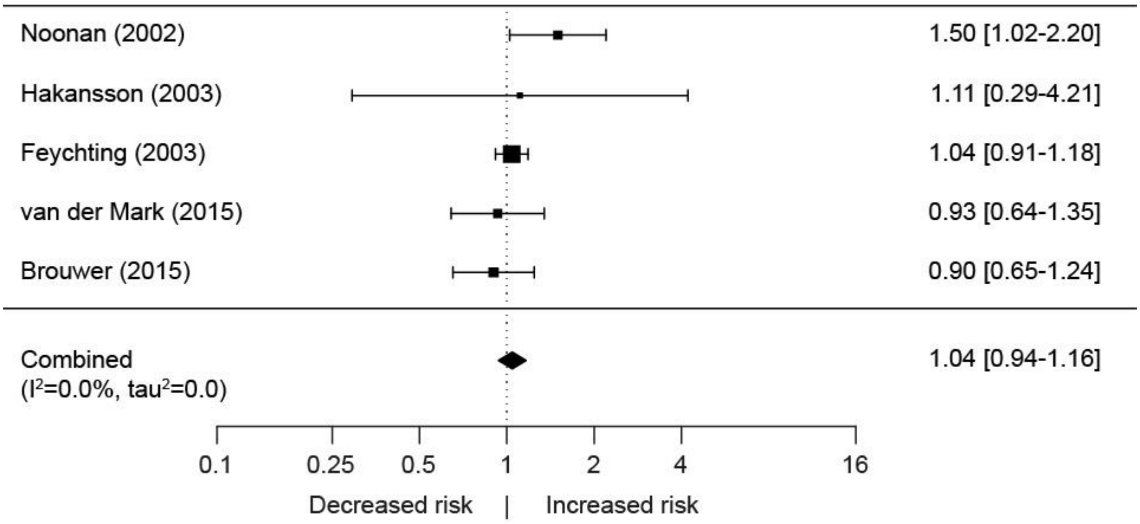


Figure 31 Meta-analysis of data on Parkinson’s disease and occupational exposure to magnetic fields - general population. Risk estimate from subanalysis of highest exposure above background levels versus background exposure.

There is insufficient data for an analysis of longest duration of exposure above background levels versus background exposure.

Industrial populations

For the studies in subjects from industrial populations, the main analysis of exposure above background levels versus background exposure shows no increased risk (figure 32).

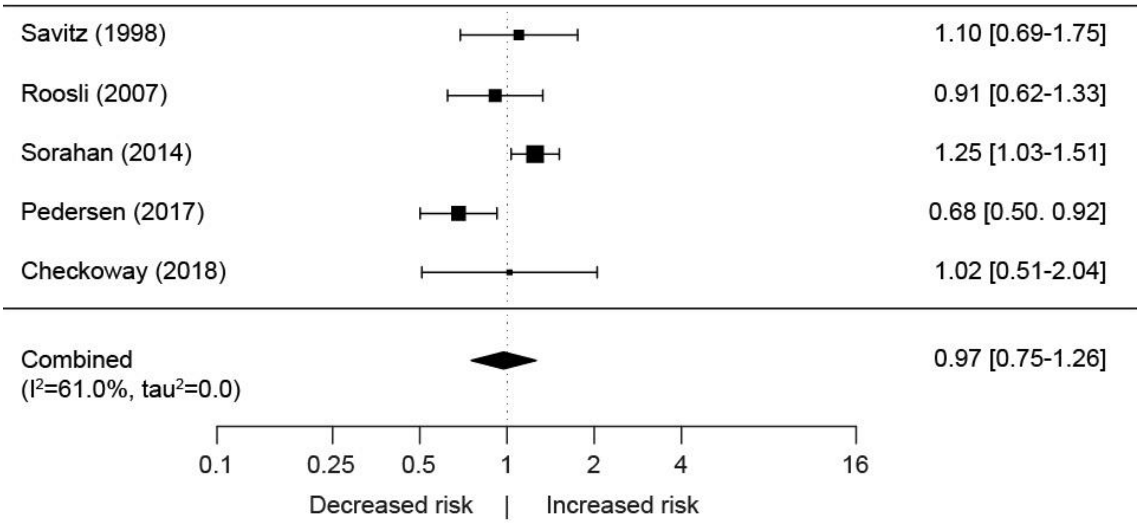


Figure 32 Meta-analysis of data on Parkinson's disease and occupational exposure to magnetic fields – industrial populations. Risk estimate from main analysis of exposure above background levels versus background exposure.

Due to the low number of studies in subjects from industrial populations, subanalyses were not possible.

Summary

Table 21 summarises the results of the meta-analyses.

Table 21 Analysis of data on the association between occupational exposure to magnetic fields and risk of Parkinson's disease

Main analysis or subanalysis	Data analysed	Risk estimatea	95% confidence interval	Number of studies	Hetero-geneity
Main analysis of general population	Exposure above background levels	1.03	0.95 – 1.11	7	56.7%
Subanalysis 1: disease	Parkinson's	1.02	0.95 – 1.11	6	61.0%
Subanalysis 1: disease	Parkinson's primary and secondary cause	--	--	1	--
Subanalysis 2: recording of disease	Incidence	--	--	1	--
Subanalysis 2: recording of disease	Mortality	1.05	0.98 – 1.12	6	38.9%
Subanalysis 3: determination of exposure	Calculated/ measured	1.04	0.91 – 1.19	5	65.5%
Subanalysis 3: determination of exposure	Works in an electrical occupation	--	--	2	--
Subanalysis 4: occupational history	Incomplete	1.05	0.97 – 1.12	5	0.0%
Subanalysis 4: occupational history	Complete	--	--	2	--
Subanalysis 6: level of exposure	Highest exposure	1.04	0.94 – 1.16	5	0.0%
Main analysis of industrial populations	Exposure above background levels	0.97	0.75 – 1.26	5	68.0%

[a] Statistically significant values are shown in bold.
Underlined values are included in the main report.

7.3.4 Experimental studies

Two publications were found on animal research on the association between exposure to ELF magnetic fields and health effects.[81,82] Both investigated the effect of implantation in laboratory animals of mesenchymal stem cells exposed in culture to 0.4-1 mT fields. Parkinson's-like symptoms were reduced in both studies.

Five studies were found on cellular models for Parkinson's disease (i.e. studies of cultured cells). In two of these, no effects were found of exposure to magnetic fields[75,83] and in three studies effects were found on oxidative stress, which may indicate pathological effects.[78,84,85] At 1 or 2 mT, the exposure levels were high compared to residential or occupational exposure.

7.4 Multiple sclerosis (MS)

7.4.1 Distance from home to high-voltage power lines

Two studies were found that investigate the association between the distance from the residence to high-voltage power lines and the occurrence of MS. No meta-analyses were therefore carried out. The risk estimates (with 95% confidence interval) from the studies are:

- <50 m: 1.19 (0.30-4.79)[2]
- 50-200 m: 1.45 (0.88-3.39)[2]
- 200-600 m: 1.16 (0.89-1.51)[2]
- <50 m: 1.03 (0.67-1.58)[4]
- 50-<200 m: 1.06 (0.90-1.24)[4]
- 200-<600 m: 1.03 (0.95-1.12)[4]

7.4.2 Residential exposure to magnetic fields

No studies were found that investigate the association between residential exposure to magnetic fields and the occurrence of MS.

7.4.3 Occupational exposure to magnetic fields

Three studies were found that investigate the association between occupational exposure to magnetic fields and the occurrence of MS. One of these is a study in subjects from the general population and two are studies in subjects from an industrial population. No meta-analyses were therefore carried out. The risk estimate (with 95% confidence interval) from the study in subjects from the general population is:

- Exposure above background levels (calculated by the Committee): 0.73 (0.40-1.34)[24]

The risk estimates from the studies in subjects from an industrial population are:

- Exposure above background levels (calculated by the Committee): 1.39 (0.23-8.38)[25]
- Exposure above background levels: 1.05 (0.64-1.74)[27]

7.4.4 Experimental studies

No experimental studies were found on the association between exposure to ELF magnetic fields and the occurrence of MS.

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