Modeled and perceived RF-EMF exposure from mobile phone base stations in relation to symptom reporting

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De rol van gemodelleerde en gepercipieerde blootstelling aan RF-EMF van zendmasten voor mobiele telefonie in het rapporteren van gezondheidsklachten

(met een samenvatting in het Nederlands)

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General introduction

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1.0. General introduction

Presently, most people in the Netherlands own a smartphone, that can be used not only for phone calls, but also for texting, internet use, navigation, etc. Over the past few decades there has been a large increase in the use of mobile phones. To facilitate mobile communication, the number of mobile phone base stations has grown simultaneously. Currently, there are about 43933 antennas for mobile phone use in the Netherlands, compared to 25002 in January 2012 (1). These base stations emit radiofrequency electromagnetic fields (RF-EMF). Many people in Europe (about 33%) are concerned about the potential health risks of this new exposure in their residential environment (2–4). Besides health concerns, some people also report non-specific symptoms such as headaches or dizziness, that they attribute to electromagnetic fields (EMF) exposure. Both biological and psychosocial processes could play a role in symptom reporting related to RF-EMF. Currently, there is ongoing debate regarding the potential health effects of this new environmental exposure, in society, as well as among scientists. The relation of mobile phone base station exposure to perceptions of exposure, perceptions of health risks, and effects on symptoms, is a complex and multifaceted topic that will be studied in this thesis. To overcome the limitations of previous studies, a multidisciplinary approach will be used, applying insights and methods from both epidemiological and psychosocial research.

1.1. Potential health effects of RF-EMF exposure

Epidemiological evidence for health effects of RF-EMF from mobile phone base stations

Epidemiological studies that focused on exposure from RF-EMF from mobile phone base stations often focused on symptom based health outcomes, rather than carcinogenic risks or chronic diseases (5). An important reason for studying symptom based health outcomes is that these are the health problems reported by people who identify themselves as electro hypersensitive (EHS). EHS is not an official medical diagnosis, and is instead self-reported by people with health problems that they attribute to electromagnetic fields (EMF) exposure. Many people with EHS claim that they can sense when they are exposed to EMF, although experimental studies, to date, were not able to identify individuals who were able to accurately indicate when exposed to EMF (6, 7). There is a lot of variation in the health problems reported by people with EHS, but among the symptoms often reported are severe headaches, sleep disturbance, and fatigue (8, 9). The health problems experienced by this group can in some cases severely limit daily functioning. Several studies examined the potential link between RF-EMF exposure and the development of non-specific symptoms. Systematic reviews (5, 10, 11) indicated the absence of a relationship between exposure and acute symptom development, but there is insufficient evidence (12) to draw firm conclusions about long term effects on non-specific symptoms, resulting from low RF-EMF exposure levels in the residential environment.

Other epidemiological evidence

For most people, RF-EMF from mobile phone base stations makes up a smaller portion (13%) of the total RF-EMF exposure than personal mobile phone use (37.5%) (13). Therefore, many epidemiological studies focus on health effects of mobile phone use rather than of mobile phone base station exposure. For mobile phone use, the head is the most localized exposure target region, and many studies have focused on associations with brain tumors (14–16). Some of these studies found associations between long term mobile phone use and brain tumors. However, other studies did not find such effects. It is difficult to reach a definite answer as to whether RF-EMF exposure from mobile phone use can cause brain tumors because of the potentially long lag periods between exposure and development of brain tumors, the difficulty to characterize long term exposure, rapid technological changes, and rarity of brain tumors. If such effects do exist, they cannot be directly equated to health effects of RF-EMF exposure from mobile phone base stations. It is important to study health effects of RF-EMF from mobile phone base stations separately from effects of other RF-EMF sources, as there may be different health effects, because the exposure is not localized in the head region, and because the exposure levels are different. In addition, for individuals without a mobile phone (mainly young children and elderly), RF-EMF from mobile phone base stations can make up a large percentage of the total RF-EMF exposure. Although overall RF-EMF exposure for these groups may be lower, young children and elderly could be more sensitive groups for developing health effects.

1.2. Reasons for uncertainty regarding health effects

Despite the available body of experimental and epidemiological evidence, there is still scientific uncertainty regarding the evidence for health effects of exposure to RF-EMF from mobile phone base stations. There are a number of different reasons for the continued scientific uncertainty that will be discussed in this thesis:

Exposure assessment

First, exposure assessment to RF-EMF from mobile phone base stations is difficult because of large spatial variation in exposure levels. Outside, but also within buildings, and even within rooms there can be a lot of variation, because RF-EMF waves are attenuated when they encounter walls or metal objects. When exposure assessment is inaccurate, studies will have insufficient statistical power to find potential health effects. Although personal measurements can be an accurate method to assess exposure, these are not feasible for large scale epidemiological studies with thousands of participants across the country. For this reason, many studies have used models to estimate exposure to RF-EMF from mobile phone base stations. In this project, the NISMap model (17, 18) will be used. This model uses 3D topography, 3D building data, and detailed information on transmitters to estimate RF-EMF levels. Validation studies (19–21) have shown that NISMap is capable of adequately ranking indoor and outdoor locations on relative exposure levels in the Netherlands. When models such as NISMap are to be used for exposure assessment in epidemiological studies, there is another source of variation that must be considered. People typically spend 65-75% of their time at home, most of this time (slightly more than 8 hours) in their own bedroom (22–24). The remaining time is spent outside of the home, for travelling, work, leisure, etc. However, there is a lot of temporal and individual variation in the amount of time people spend at home, depending on for example the weather (rain, temperature, etc), but also employment characteristics, and size of the home (22). RF-EMF exposure from mobile phone base stations is usually modelled at the home address, ignoring the time people spend at other locations. In theory, it would be possible to model exposure at locations other than the home address, if the floor height, address and time spent there are known, and if the surface area of the address is not too large (because of the spatial variation in RF-EMF levels). In practice, it is often difficult to obtain the required data and therefore it is likely to be more efficient to estimate exposure at the home address. Chapter two and three of this thesis will examine the applicability of modelled exposure at the home address for accurate and efficient exposure assessment in epidemiological studies.

Lack of longitudinal data

Secondly, many prior studies have been cross-sectional or experimental, as longitudinal projects are costly. This limits the causal inference of associations, as temporal precedence cannot be studied in cross-sectional studies. Temporal precedence is a requirement for proving causal associations. In cross-sectional studies, it is often not possible to fully exclude alternative explanations (for example reversed causation) for associations between determinants and health outcomes. A disadvantage of experimental studies is that they can only study short term effects, and that the results of such studies cannot easily be generalized to an actual population context. This thesis will include analyses on RF-EMF and health outcomes in the longitudinal AMIGO cohort, which will be described in chapter five and seven.

Uncertainty about relevant health outcomes

Thirdly, not much is known about potential biological mechanisms through which RF-EMF could cause health problems. Prior studies have established that high intensity RF-EMF may lead to an increase in body temperature (25), damaging body tissue. Based on this effect, many countries have set exposure limits for RF-EMF. In the everyday environment total exposure levels are much lower than these limits (average exposure levels less than 1% of limits) (13, 26). There may be other biological mechanisms than tissue heating through which health effects could occur, but there is currently no conclusive evidence for such mechanisms to occur in humans at everyday levels of exposure. As a result of this knowledge gap, it is also a challenge to determine which health outcome measures should be studied. For non-specific symptoms, it is unclear which symptoms should be studied specifically and how the outcome measures should be constructed. Chapter four of this thesis examines the underlying factor structure of self-report symptom questionnaires and compares different methods to construct and analyze symptom scores.

Role of psychosocial mechanisms

Finally, as many studies did not include information about perceptions of exposure and perceived health risks, it was not possible to rule these perceptions out as an alternative explanation, nor to examine indirect effects of actual exposure on health through perceptions. Some studies looked at effects of risk perception on symptom reporting, but often these studies do not consider the potential role of actual exposure simultaneously. Also, there have been few longitudinal studies in the general population. In chapter four we will study associations between both modelled and perceived RF-EMF exposure to mobile phone base stations in relation to symptom reporting. Chapter six will evaluate the impact of different perceptions about exposure and health risks on health outcomes for participants with different subject characteristics. Chapter seven will examine whether the role of modelled and perceived exposure in symptom reporting is similar for different types of environmental health risks.

1.3. Psychosocial mechanisms

People form mental models of base stations in their living environment. Mental models are internal representations of the external reality that allow individuals to interact with the world (27, 28). These models shape reasoning, decision making, and behavior and can play a role in individual health responses to the environment. Mental models of base stations can include beliefs about exposure and potential health risks (29–31). Such beliefs can influence the way people interpret new information about health risks, but also the way they think about the cause of somatic symptoms (32, 33). Prior research has linked risk perception and concerns about potential health risks of new technologies to increased somatic symptom scores, health care use, and a decreased quality of life (33–36). It is thought that perceptions about exposure and perceptions of health risks and concerns can also be important in the case of RF-EMF from mobile phone base stations, aside from, or in combination with a potential influence of actual exposure, which will be studied in chapter four.

Characteristics of a risk

The introduction of new technologies in the environment often leads to concerns about potential health risks. There are a number of known risk characteristics that influence risk perception. A few decades ago, influential studies (37, 38) highlighted discrepancies between the perception of risks by the general population and actual risks. A number of characteristics of a hazard were shown to influence risk perception: 1) voluntariness of the exposure, 2) immediacy of the consequence, 3) whether the risk was known precisely by the exposed person, 4) chronic versus catastrophic effect, 5) dread, 6) severity of consequences (fatality), 7) to what extent the risk is known to science, 8) perceived control over exposure, 9) novelty of the risk. In the case of RF-EMF exposure from mobile phone base stations, this exposure is involuntary, people are often uncertain about what the risks could be, there is uncertainty among scientists, people do not have control over their exposure, and it is a relatively new technology. All these factors explain why many people are concerned about the potential health risks of mobile phone base stations. People are generally less concerned about the health risks of the use of their own mobile phones, and continue to use these devices, despite the fact that for most adults RF-EMF exposure from own mobile phone use is higher than from mobile phone base stations. Characteristics such as the voluntariness, and control over exposure are likely to play a role. Despite the observation that many of the above mentioned risk characteristics apply for mobile phone base stations, a study among the New Zealand population (39) showed that people were more concerned about other environmental risks such as air pollution or pesticides than about mobile phone base stations, for which many of the characteristics mentioned above apply as well. Chapter seven compares the role of risk appraisal in symptom reporting for different type of environmental exposures (RF-EMF, noise, air pollutants), taking the actual (modelled) exposures into account.

Subject characteristics

Aside from characteristics of a risk, there are other factors that could affect how people perceive potential risks. Cultural, political, and sociological factors may play a role. For example, a study (40) in Bangladesh found that people interpreted the presence of mobile phone base stations as a sign of economic progress, rather than as a potential health risk. Although many factors can be important, this thesis will focus on subject characteristics such as gender and education. Subject characteristics can influence how people perceive potential risks, but they could also influence the degree to which someone experiences somatic symptoms, or the associations between perceptions and symptoms. These topics will be studied in chapter six. People may also worry about other aspects of mobile phone base stations, rather than health risks. For example, the placement process of a new antenna in a residential area may be perceived as unfair, and people might worry about property values (41). Such concerns are not the focus of this thesis, but may contribute to distrust in the responsible authorities regarding mobile phone base stations, and less trust in official reports that communicate absence of health effects.

Mechanisms

Chapter six will examine the temporal directionality of associations between risk appraisal and symptom reporting. Studying the temporal directionality of associations can improve our understanding of which underlying psychosocial mechanisms are important. Understanding the underlying psychosocial mechanisms is important to develop effective risk communication strategies, but also to interpret the effects of epidemiological studies and the role of perception. There is evidence for the existence of nocebo effects through expectations of negative health effects from EMF exposure. A nocebo response is the counterpart of placebo, i.e. an adverse health response after a treatment or exposure that is not a direct result of this exposure, (42). A self-reinforcing circular process may occur through somatosensory amplification, especially in people who report electro hypersensitivity (43, 44). A lot of research into psychosocial mechanisms has been done in laboratory experiments. Although experimental studies have shown that nocebo mechanisms can be responsible for an increase in symptoms after a change in the environment through expectations of negative health effects, it is still not fully understood to what extent this mechanism is responsible for the associations between risk appraisal and symptom based health outcomes in the general population. Therefore, more research is needed in a general population context, as the relevance of such mechanisms in a general population context is difficult to study in experimental studies. In exposed general population samples other mechanisms may be important as well, such as reversed causation mechanisms where people become more aware of environmental exposures as a potential cause of existing or new symptoms, which has been described as environmental monitoring and incorrect attribution (45, 46). The relative importance of different psychosocial mechanisms can have implications for the effectiveness of different risk communication strategies in preventing unnecessary concerns and increased symptom reporting.

1.4. The AMIGO participants

The chapters three to six all study data from the Dutch population-based Occupational and Environmental Health Cohort study (AMIGO) (47) to study associations between modelled exposure, perceptions and symptom based health outcomes. The AMIGO cohort was setup to longitudinally study occupational and environmental determinants of diseases and wellbeing in The Netherlands. The recruitment strategy and population characteristics were described in detail in (47). All participants were adults, between 31 and 65 years old at the time of enrollment. Participants were recruited through an invitation from their general health practitioner. The general practitioners were part of a network for primary healthcare at the Netherlands institute for Health Services Research (NIVEL). The cohort members were invited to fill in online questionnaires, see Figure 1 for the timeline. 14829 Cohort members (16% of those who were invited) filled in the online baseline questionnaire in 2011 or 2012. A subsample of the AMIGO participants was invited to participate in additional follow-up questionnaires in 2013 (n=3999 invited, 2228 participants) and in 2014 (n=2228 invited, 1740 participated). All AMIGO baseline participants were invited for a follow-up questionnaire in 2015 (n=7905 participated).

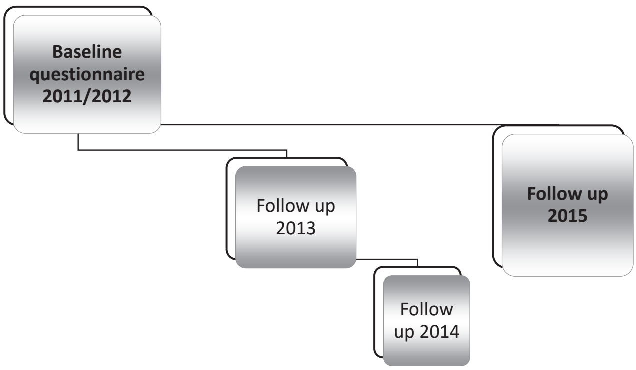

Figure 1. Timeline questionnaires

1.5. Thesis Aims and Research Questions

This thesis is divided in two parts. The first part will focus on exposure assessment of RF-EMF exposure to mobile phone base stations. The second part is about studying symptom based health outcomes in AMIGO and the associations with modelled and perceived exposures, and will also discuss the role of risk appraisal.

Aim

The overall aim of this thesis is to improve the understanding of the associations between modelled and perceived exposure to RF-EMF from mobile phone base stations in relation to self-reported health outcomes.

Research questions

1. Can a three-dimensional geospatial model (NISMap) be used to efficiently and accurately assess personal RF-EMF exposure in epidemiological studies? (Chapter 2 & 3)
2. What is the underlying factor structure of self-report symptom questionnaires and how can this structure be taken into account in epidemiological studies? (Chapter 4)
3. How are modelled and perceived exposure to RF-EMF from mobile phone base stations related to overall symptom score and sleep disturbances? (Chapter 5)
4. Can we improve our understanding of perceptions of exposure and health risks by examining cross-sectional and longitudinal associations between these perceptions and symptom scores, and what is the influence of a number of subject characteristics (sex, age, education, and trait negative affect) on risk appraisal and symptoms? (Chapter 6)
5. Do we find similar patterns of associations between modelled and perceived exposure in relation to self-reported health outcomes for air pollutants and noise from road traffic as for RF-EMF exposure of mobile phone base stations? (Chapter 7)

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Exposure assessment RF-EMF from mobile phone base stations

Validity of at home model predictions as a proxy for personal exposure to radiofrequency electromagnetic fields from mobile phone base stations

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Abstract

Background: Epidemiological studies on the potential health effects of RF-EMF from mobile phone base stations require efficient and accurate exposure assessment methods. Previous studies have demonstrated that the 3D geospatial model NISMap is able to rank locations by indoor and outdoor RF-EMF exposure levels. This study extends on previous work by evaluating the suitability of using NISMap to estimate indoor RF-EMF exposure levels at home as a proxy for personal exposure to RF-EMF from mobile phone base stations.

Methods: For 93 individuals in the Netherlands we measured personal exposure to RF-EMF from mobile phone base stations during a 24 h period using an EME-SPY 121 exposimeter. Each individual kept a diary from which we extracted the time spent at home and in the bedroom. We used NISMap to model exposure at the home address of the participant (at bedroom elevation). We then compared model predictions with measurements for the 24 h period, when at home, and in the bedroom by the Spearman correlation coefficient (r_{sp}) and by calculating specificity and sensitivity using the 90th percentile of the exposure distribution as a cutpoint for high exposure.

Results: We found a low to moderate r_{sp} of 0.36 for the 24 h period, 0.51 for measurements at home, and 0.41 for measurements in the bedroom. The specificity was high (0.9) but with a low sensitivity (0.3).

Discussion: These results indicate that a meaningful ranking of personal RF-EMF can be achieved, even though the correlation between model predictions and 24 h personal RF-EMF measurements is lower than with at home measurements. However, the use of at home RF-EMF field predictions from mobile phone base stations in epidemiological studies leads to significant exposure misclassification that will result in a loss of statistical power to detect health effects.

1. Introduction

There is ongoing concern about the potential health effects of exposure to radiofrequency electromagnetic fields (RF-EMF) from mobile phone base stations (1). Epidemiological studies to date have found only very limited evidence for any kind of health effects related to RF-EMF (2). However, uncertainties in the exposure assessment of personal RF-EMF (from all sources and sources separately) hinder reaching a more definitive conclusion about the absence or presence of any possible association between RF-EMF exposure, from for example mobile phone base stations, and health problems.

RF-EMF exposure from mobile phone base stations (in the Netherlands) contributes ~13% to total environmental RF-EMF exposure (3). This contribution may vary by location and by age groups due to differences in behavioural patterns. There is no scientific evidence for any specific biological mechanisms leading to health effects, and thus potential health effects of RF-EMF may differ across frequency bands. Therefore, it is important to study the exposure from mobile phone base stations both separately and combined. Due to the absence of a strong correlation between RF-EMF from mobile phone base stations and other RF-EMF sources (4) it is possible to study this source separately.

Several methods have been employed to assess individual exposure to RF-EMF from mobile phone base stations. Personal measurements are considered the best approach in assessing personal RF-EMF exposure (5). However, even the use of personal dosimeters has limitations that can lead to underestimation of exposure, such as body shielding, measuring multiple signals in one frequency band, and measurements below the detection limit (6, 7). Further, because of time and cost constraints personal measurements are not feasible for large scale epidemiological investigations (4). Other methods typically estimate exposure at the home address as a proxy of personal exposure. Simple methods such as the distance between nearby transmitters and the home address as a proxy of personal exposure to RF-EMF (8–10) are insufficiently accurate (4, 11). Frei et al. (2010) (4) showed that using a model to estimate exposure at the home address is currently the most appropriate method for estimating RF-EMF exposure in large epidemiological studies. In recent years several geospatial models have been developed for estimating RF-EMF exposure from mobile phone base stations at the home address (11–13).

The 3D radiowave propagation model NISMap (13) has been developed to predict RF-EMF exposure from fixed site transmitters. Previous studies (13–16) have shown that NISMap is able to meaningful rank outdoor and indoor RF-EMF exposure levels from mobile phone base-stations. Spearman correlations for total mobile phone downlink (hereafter referred to as downlink) RF-EMF between predicted values and spot measurements were around r_{sp} =0.7. However, people are not always at their home address, and the amount of time they spend at home can vary between individuals and different time periods (17, 18). Therefore, a model estimating RF-EMF for the home address may not be sufficiently accurate to predict personal exposure to RF-EMF from base stations. Limited work has been done to validate the estimation of personal RF-EMF exposure from base-stations based on spatial models. Frei et al. (2009) (20) measured personal exposure during one week for 166 subjects in Switzerland. They compared personal RF-EMF exposure measurements from all far field sources (including FM, TV, Tetrapol, mobile phone uplink (hereafter referred to as uplink), downlink, DECT, W-LAN) with NISMap model predictions of exposure to fixed site transmitters (FM, TV, Tetrapol, mobile phone base station downlink). They reported a Spearman correlation of 0.28 (CI 95%: 0.14-0.42) between measured and modelled values (4). As in the end health effects are driven by the individual exposure experience there is a clear need for additional studies on the suitability of using at home modeling of RF-EMF for approximating personal exposure to RF-EMF from base stations. In this study we extend on previous observations by evaluating whether at home modelled RF-EMF exposure by NISMap has a good correlation with personal measurements, and whether it is a valid proxy for 24 h personal exposure to RF-EMF from base stations.

2. Material and Methods

2.1 Population

The selection method and exclusions are described in more detail in Bolte & Eikelboom (2012) (3). In short, we invited 3000 adult (18+) members from an internet panel (TNS-Nipo) living in the north-west of the Netherlands. The panel members were approached by email to fill out a questionnaire and carry a measurement device for 24 hours. This resulted in a positive response of 909 persons from which 140 were selected (based on variation in features such as sex, age, social economic status, employment and residential area) to participate in the measurements. The measurements took place in 2009 and 2010 and continued until 100 complete measurement datasets were collected. After excluding participants with incomplete diary data, 98 participants with complete measurement data were retained (age range: 18-82 years). Five participants were excluded because we could not estimate the field strength for their home address due to missing input data, resulting in a total of 93 participants with both model estimates as well as personal measurements.

2.2 Model description and model input

For each participant we estimated RF-EMF exposure at the home address (at bedroom elevation) using the NISMap model. We did not model the exposure at work, as subjects in general spend less than 30% of their time at work and because the work address was not known for all participants. Additionally, some of the participants have professions that are not bound to one location, f.i. driver or builder.

NISMap is a three dimensional radiowave propagation model that uses detailed information about antenna location and radiation patterns, 3D building data and topography to compute the field strength of the downlink sources of different frequencies (UMTS, GSM900, GSM1800). The Double Power Law (21) radio wave propagation algorithm used previously by (14–16) was used to calculate the decrease of RF-EMF with distance. NISMap allows to set building damping values to correct for the attenuation of radio waves by buildings. We set the damping of roofs to 4.5 dB, damping of walls to 3 dB and the inside damping to 0.6 dB/m for all buildings. These values are similar to values used in earlier studies (14–16). Individual building characteristics such as the type of wall material were not used as input data for the model, as a previous study found that inclusion of these predictors did not significantly improve model prediction in the Netherlands most likely because of the relative homogenous building characteristics (15). A technical description of the model can be found in (13, 16).

The coordinates of the participants' home addresses were obtained from the Dutch Cadastre in 2012 (BAG, Basisregistraties Adressen en Gebouwen). The Dutch Radiocommunications Agency (Agentschap Telecom) provided us with detailed information about transmitters (2011), such as the coordinates, beam direction, and height of the transmitter. We created a 3D box model of all buildings in the Netherlands, by combining data on the building locations and outline from the national BAG building data set with height information from the Netherlands elevation model (Actueel Hoogtebestand Nederland 2, AHN2). The bedroom elevation was used as input for the model, as participants generally spend most of their time in their bedroom while they are at home. To obtain the bedroom elevation we asked participants the floor number of their bedroom (where ground level counts as zero). We assumed a floor height of 3 meters per floor. If this resulted in an estimation of the bedroom elevation larger than the total building height (n=5) we subtracted 1.5 meters from the total building height and used that value as an estimate of bedroom elevation.

2.3 Exposure assessment

We used the EME-spy 121 (Satimo, Cortaboeuf, France, http://www.satimo.fr) to measure the RF electric fields in 12 frequency bands (FM radio (88–108 MHz), TV3 (174–233

MHz), TETRA (380–400 MHz), TV4&5 (470–830 MHz), GSM 900 uplink (880–915 MHz), GSM 900 downlink (925–960 MHz), GSM 1800 uplink (1710–1785 MHz), GSM 1800 downlink (1805–1880 MHz), DECT (1880–1900 MHz), UMTS uplink (1920–1980 MHz), UMTS downlink (2110–2170 MHz), WiFi (2400–2500 MHz)), with the sampling frequency set to every 10^{th} second. The upper detection limit of the device is 265 mW/m² (10 V/m). The lower detection limit is 0.0066 mW/m² (0.05 V/m).

Participants were asked to carry the measurement set continuously for 24 h, except when they were sleeping or during activities where it would not be safe for the participant to wear the device or the device would be at risk of being damaged (such as showering, sports). Participants carried the EME-SPY in a camera bag strapped over their left shoulder and clipped on the right hip to the belt. At night, the exposimeter was positioned on the bedside table next to the head, with the blue side, containing the antennae, directed towards the window.

Participants filled in a time activity diary, where they described their activities during the measurements, including mobile/cordless phone use, as well as all unexpected or notable events such as not being able to wear the measurement set during a specific time window. More information about the exact procedure can be found in Bolte and Eikelboom (2012).

2.4 Data-analysis

A calibration correction for each exposimeter was applied to all measurements, based on calibration tests in a GTEM (Gigahertz Transverse ElectroMagnetic cell) and an Open Area Test site (6). Downlink measurements may be slightly influenced by out-of-band signals such as DECT (6). We therefore removed the measurements during time spent on DECT cordless phones. We then computed the total downlink exposure by summing power density (W/m²) of the GSM900 downlink, GSM1800 downlink and UMTS downlink frequencies for the measurements and the model predictions (results per downlink frequency in the Appendix, Table A.1.). Based on the activity diary, all measurement data were placed in three different categories: in bedroom, at home, overall 24 h. Statistics per category (bedroom / at home /overall 24 h) were calculated by pooling all available measurements per category.

Because the detection limit of the exposimeter is relatively high compared to exposure values in a home environment there was a large percentage (GSM900 83%, GSM1800 90%, UMTS 96%, total downlink 78%) of measurement data below the detection limit. We used robust regression on order statistics (ROS) to impute measurement values below the detection limit, which has been shown to be an reliable method for this type of data (22).

We computed several indicators to determine the accuracy of the NISMap model predictions: The mean modelled and measured values, the ratio (mean modelled value divided by the mean measured value), the mean difference between modelled and measured values (modelled - measured), the mean relative difference (mean difference divided by the average of measured and modelled values), precision (the standard deviation of differences between modelled and measured values), the coefficient of variation (ratio of the standard deviation to the mean) and the Spearman rank correlation (r_{sp}) between modelled and measured values. In order to calculate sensitivity and specificity parameters we dichotomized the modelled and measured values with a cutoff percentile of 90% based on distributional plots. All analyses were carried out using the statistical program R (3.1.0).

3. Results

3.1 Descriptive statistics

The mean age of the 93 participants, 45 men and 48 women, was 44.3 years (range: 19–81, standard deviation: 16.2). Participants spent on average 16.8 h (standard deviation: 3.9) at home, of which 7.3 h (standard deviation: 1.93) in the bedroom. The majority of participants did not work on the day of the measurements (worked: n=36, not worked: n= 57). There was a large variation in home types (detached/semi-detached home: n= 25, terraced home: n=28, large apartment: n=15, small apartment: n=25) as well as degree of urbanisation (downtown urban area: n=21, urban outskirts: n=27, urban green area: n=17, village: n=28).

3.2 Accuracy of model predictions

Table 1 shows the accuracy of the model predictions (see appendix table A.1 for results per frequency band). The mean modelled value for the 24 h period was 0.039 mW/m², the mean measured value 0.023 mW/m². We found a Spearman correlation of 0.36 between modelled and measured values for the 24 hour period. The statistics restricted for time spent at home (mean measured: 0.017 mW/m²) and time spent in the bedroom (mean measured: 0.018 mW/m²) were similar but with somewhat higher Spearman correlations (at home r_{sp} = 0.51; bedroom r_{sp} = 0.41). The sensitivity of the model predictions for the total 24 h period was 0.30 (CI 95% = 0.07-0.65), the specificity of the model predictions was 0.92 (CI 95% = 0.83-0.97). In figure 1 we show two Bland-Altman plots (23) for the absolute and the relative differences between the NISMap

Table 1. Accuracy of model predictions for the total downlink RF-EMF of all mobile phone base stations (unit: mW/m^2) for the 24 h period, time spent at home and in the bedroom

	24 h overall	At home	In bedroom
Mean modelled*	0.039	0.039	0.039
mean measured	0.023	0.017	0.018
ratio model/measured	1.713	2.356	2.212
median measured	0.011	0.004	0.000
mean difference (modelled-measured)	0.016	0.022	0.021
mean relative difference	0.525	0.808	0.755
Precision (sd difference)	0.102	0.102	0.099
Coefficient of variation	4.470	6.129	5.572
Spearman r	0.36	0.51	0.41
Sensitivity 90% cutoff and 95% confidence intervals	0.30 (0.07-0.65)	0.30 (0.07-0.65)	0.40 (0.12-0.74)
Specificity 90% cutoff and 95% confidence intervals	0.92 (0.83-0.97)	0.92 (0.83-0.97)	0.93 (0.85-0.97)

*This value is equal for each category because we only model exposure for the home address at bedroom elevation.

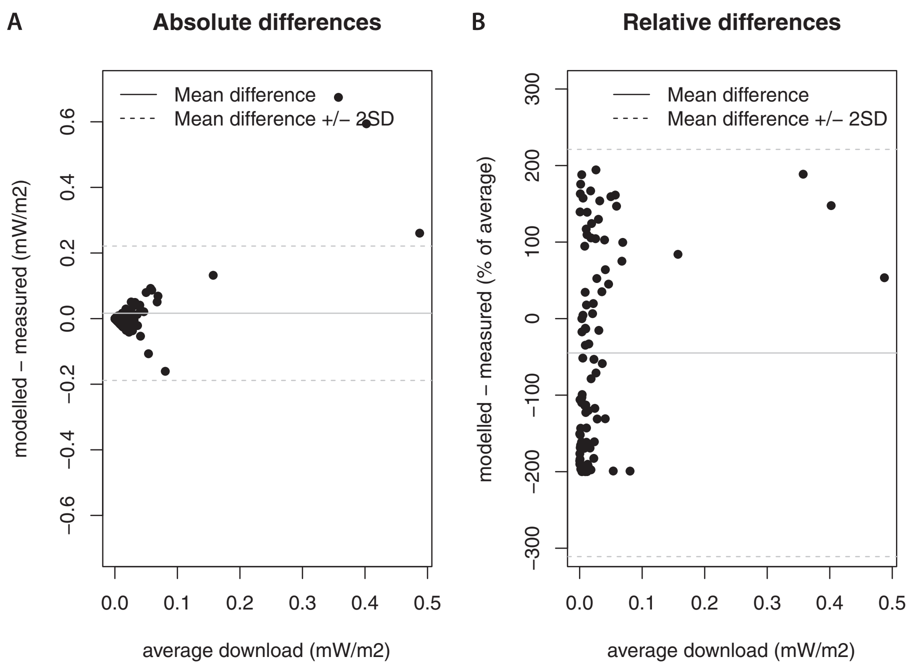

Figure 1. Bland–Altman plot of the mean downlink RF-EMF, showing the absolute (A. left) and relative (B. right) differences between modelled and measured values for the 24 h period. The solid line shows the bias and the striped lines the bias ±2 standard deviations.

model predictions and the 24 h overall measurements. We observe large differences between modelled and measured RF-EMF levels, with both an over- and underestimation. However, on average there is indication of an overestimation of the model of the absolute levels (Table 1, Figure 1). An extra analysis where we stratified by the subjects that did not work during the measurement data (n=57) and subjects that did work during the measurement day showed a slightly higher Spearman correlation for subjects who did not work (not worked: $r_{sp} = 0.39$, worked: $r_{sp} = 0.32$).

4. Discussion

In this study we evaluated the validity of using the at home exposure (at bedroom elevation) as modelled by NISMap to assess personal exposure to RF-EMF in epidemiological studies. We compared NISMap model predictions of RF-EMF exposure from mobile phone base stations with personal measurements (downlink). We found a low to moderate Spearman correlation between model predictions and personal measurements of 0.36 for a 24 h period. As expected, these correlations are lower than correlations between model predictions at home (r_{sp} 0.51) and in the bedroom (r_{sp} 0.41).

In epidemiological studies it is important to be able distinguish between high and low exposed individuals. In our study we used the sensitivity and the specificity to evaluate how well we distinguish between exposed and non-exposed individuals (as defined by the 90th percentile of the empirical distribution). We found a high specificity (0.9) of the NISMap model, but a relatively low sensitivity (0.3). An ideal model would have a high specificity as well as a high sensitivity. However, for epidemiological studies with rare exposures, such as high exposure to RF-EMF, a high specificity is more important than a high sensitivity. Neubauer et al. (2007) (5) have demonstrated that, if an association exists, low specificity leads to a greater risk bias and therefore less power to detect potential health effects. The effect of low sensitivity on the risk bias is much smaller.

Frei et al. (2010) (4) also assessed the performance of the NISMap model in predicting personal RF-EMF exposure in Switzerland. Frei and colleagues modelled all fixed site transmitters (FM, TV, Tetrapol, and Downlink) and compared this with measurements from all far field sources (FM, TV, Tetrapol, uplink, Downlink, DECT, W-LAN). Compared to our study they reported a slightly lower correlation of $r_{sp} = 0.28$. This might in part be explained due the fact that the comparison of Frei et al. included more RF-EMF sources in their measurements than that were used in the NISMap model. Similarly, when we compared our modelled downlink exposures to the personal measurements including all far field exposures, we obtained a correlation of $r_{sp} = 0.22$.

The studies by Bürgi (2009) and by Beekhuizen (2014) (16, 15) focused on downlink RF-EMF levels only. They compared indoor spot measurements with NISMap predictions and found Spearman correlations between 0.60 and 0.74. These values are noticeably higher than our indoor values based on personal measurements (bedroom r_{sp} 0.41; at home r_{sp} 0.51). Possible explanations might be the higher detection limit of the measurement device used in our study as well as differences in measurement method. Our subjects carried a dosimeter on their bodies and left the device on a small bedside table during nighttime. In contrast, both other studies (15, 16) used stationary spot measurements on 7 spots in the room, thereby capturing the average exposure in the room. While our method may reflect personal exposure more accurately, our measurement results could be influenced strongly by local interference patterns.

The specificity (0.90) reported in (16) is similar to our specificity for the at home measurements (0.92), although they reported a higher sensitivity (0.60 versus 0.32 in our study). These results indicate that modelling bedroom exposure at the home address as a proxy for personal exposure does not lead to a large number of 'false positives' (subjects incorrectly classified as high exposed), which is an important feature for epidemiological studies with a low prevalence of (high) exposure. However, because of the low sensitivity it will take a large sample size to detect potential health effects if they exist.

4.1 Strengths and limitations

One of the strengths of our study is the varied subject sample. The subjects vary greatly considering age, sex, employment, residential area and housing characteristics. A second strength is the detailed input data on antenna characteristics, 3D buildings and elevation used to predict exposure, as accurate and complete input data is important for the spatial modeling of RF-EMF levels (24, 25). Another strength of our study is the knowledge about the whereabouts of the subjects allowing us to compare separately between the measured exposure when at home and when in the bedroom.

One of the limitations in validation studies is the lack of a "golden standard" for estimating error in model predictions. In our study we compare model predictions to personal measurements, but even personal measurements are not a perfect reflection of true exposure. The EME Spy 121 measurement device underestimates actual exposure (6) and has a relatively high lower detection limit. Due to the large number of measurements below the detection limit our results are highly dependent on the ROS modelling. However, it has been shown that ROS is a reliable imputation method for this type of data. (22) and we therefore do not expect that the large number of non-detects influenced our results. Secondly, we estimated bedroom elevation using a rough estimate of an average floor height of 3 meter per floor multiplied with the floor number of the bedroom, leading to some error in the exact receptor height. An accurate estimation of the height is however very important for the accuracy of the model estimation (25) and this may have led to a decrease in model performance. Finally, for this study we used antenna data from 2011 as input data for the prediction model. The measurements were taken earlier, in 2009 and 2010. For an optimal comparison the information about location and characteristics of the antenna should be dated as closely to the date of the measurements as possible.

4.2 Considerations for future research

The use of models to predict personal exposure to RF-EMF has limitations due to the large spatial variation in RF-EMF levels in combination with subject movement patterns. Misclassification can lead to significant problems in epidemiological studies that look at an association between RF-EMF exposure and possible health effects, as potential health effects might not be detected due to lack of power and attenuated effect sizes (26). However, there are currently no alternatives for geospatial models to predict exposure for large scale epidemiological studies. Some improvements might be made by modelling additional locations where participants spend a lot of time like work or school, but future studies are necessary to assess the potential added value of this approach. It should be noted that detailed location information of the participants within buildings such as schools and offices are needed to reliable model RF-EMF exposure due to the large spatial variation in RF-EMF levels. This information is often not readily available, making it difficult to include these locations in estimating total exposure. When we stratified our analyses by the subjects that did not work during the measurement day (n=57) and subjects that did work during the measurement day we observed a slightly higher Spearman correlation for subjects who didn't work (not worked: r_{sp} = 0.39, worked: r_{sp} = 0.32). Note that the low to moderate association between modelled exposure to RF-EMF from mobile phone base stations and measured personal exposure is similar to the accuracy found for other environmental pollutants, most notably air pollution (27, 28). Despite the presence of misclassification, a large number of air pollution studies have found health effects, although the type of exposure and health effects expected for air pollution are very different than for RF-EMF. When epidemiological studies have a sufficient sample size it should be possible to pick up potential health effects of RF-EMF exposure using NISMap.

4.3 Conclusion

This study evaluated the use of NISMap to predict personal exposure to RF-EMF from mobile phone base stations. The results indicate that a meaningful ranking of personal RF-EMF can be achieved, even though the correlation between model predictions and

24 h personal RF-EMF measurements is lower than with at home measurements. Our results indicate significant misclassification of participants, although in part our low Spearman correlations and sensitivity parameters can be explained by the inherent measurement error in the personal RF-EMF measurements. Exposure misclassification, assuming a classical error structure, leads to loss of power and can lead to attenuation of effect sizes (29). The main implication of our findings is therefore that epidemiological studies of health risks from far field RF-EMF will need a large number of participants in order to have sufficient power for detecting potential health effects. Ideally, we would use more accurate methods of exposure assessment, but such methods (personal measurements, modelling multiple locations where the participants spend a lot of time, or including behavioral characteristics and other RF-EMF sources in the exposure model) are often expensive or require information that is not readily available.

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Appendix

Table A.1 Accuracy of model predictions for GSM, DCS, UMTS and total downlink RF-EMF of all mobile phone base stations (unit: mW/m2) for 24 h overall, time spent at home, and in the bedroom.

	24 h overall				At home				In bedroom			
	GSM	DCS	UMTS	Total down-link	GSM	DCS	UMTS	Total down-link	GSM	DCS	UMTS	Total down-link
Mean modelled	0.017	0.015	0.007	0.039	0.017	0.015	0.007	0.039	0.017	0.015	0.007	0.039
Mean measured	0.007	0.014	0.002	0.023	0.006	0.010	0.001	0.017	0.006	0.011	0.001	0.018
Ratio modelled/ measured	2.405	1.068	4.227	1.712	2.981	1.536	6.346	2.356	2.969	1.408	5.548	2.122
Median measured	0.003	0.004	0.001	0.011	0.000	0.000	0.000	0.004	0.000	0.000	0.000	0.000
mean difference (modelled-measured)	0.010	0.001	0.005	0.016	0.011	0.005	0.006	0.023	0.011	0.004	0.006	0.022
Mean relative difference	0.825	0.065	1.235	0.525	0.995	0.423	1.455	0.808	0.992	0.339	1.389	0.755
Precision (SD difference)	0.075	0.053	0.018	0.102	0.074	0.054	0.018	0.102	0.073	0.058	0.017	0.099
Coefficient of variation	10.558	3.770	10.804	4.470	13.038	5.452	15.990	6.129	12.805	5.365	12.943	5.572
Spearman R	0.323	0.269	0.173	0.361	0.426	0.522	0.428	0.511	0.413	0.327	0.362	0.410

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Residential exposure to RF-EMF from mobile phone base stations: model predictions versus personal and home measurements

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3

Graphical Abstract

1. The population is exposed to RF-EMF from mobile phone base stations.

2. We modelled exposure for 9563 addresses and invited 276 households with large exposure contrast to participate.

3. We compared model predictions at the home address and personal 48 hour measurements for 47 participants.

4. We found a moderate correlation between model predictions and 48 hour measurements (R_{Sp}= 0.47).

Abstract

Introduction: Geospatial models have been demonstrated to reliably and efficiently estimate RF-EMF exposure from mobile phone base stations (downlink) at stationary locations with the implicit assumption that this reflects personal exposure. In this study, we evaluated whether RF-EMF model predictions at the home address are a good proxy of personal 48h exposure. We furthermore studied potential modification of this association by degree of urbanisation.

Method: We first used an initial NISMap estimation (at an assumed height of 4.5 m) for 9,563 randomly selected addresses in order to oversample addresses with higher exposure levels and achieve exposure contrast. We included 47 individuals across the range of potential RF-EMF exposure and used NISMap to re-assess downlink exposure at the home address (at bedroom height). We computed several indicators to determine the accuracy of the NISMap model predictions. We compared residential RF-EMF model predictions with personal 48h, at home, and night-time (0:00-8:00 AM) ExpoM3 measurements, and with EME-SPY 140 spot measurements in the bedroom. We obtained information about urbanisation degree and compared the accuracy of model predictions in high and low urbanized areas.

Results:
We found a moderate Spearman correlation between model predictions and personal 48h (r_{Sp}=0.47), at home (r_{Sp}=0.49), at night (r_{Sp}=0.51) and spot measurements (r_{Sp}=0.54). We found no clear differences between high and low urbanized areas (48h: high r_{Sp}=0.38, low r_{Sp}=0.55, bedroom spot measurements: high r_{Sp}=0.55, low r_{Sp}=0.50).

Discussion:
We achieved a meaningful ranking of personal downlink exposure irrespective of degree of urbanisation, indicating that these models can provide a good proxy of personal exposure in areas with varying build-up.

1. Introduction

There has been a widespread increase in exposure to radiofrequency electromagnetic fields (RF-EMF) in recent decades due to the rise of mobile phone use and developments in communication technology (1, 2). Potential risks from modern technology can lead to concern within the general public, especially when exposure is perceived as unavoidable and uncontrollable (3), such as the potential health risk of exposure to RF-EMF from mobile phone base stations (4). As a result, several studies addressed the possible association between RF-EMF exposure and development of various health problems (e.g. (5, 6)) If such health effects exist, they are likely to be small, and therefore accurate and efficient RF-EMF exposure assessment for large populations is essential for epidemiological studies (7).

RF-EMF exposure from mobile phone base stations is difficult to assess because of the large 3D spatial variation in exposure patterns and subject movement patterns. Personal measurements are at present not feasible for large epidemiological studies due to time and cost constraints, and therefore models are needed to accurately and efficiently estimate exposure. The geospatial model NISMap (8, 9) was developed to efficiently estimate exposure from fixed site transmitters. Validation studies (8–11) found a reasonably good agreement (Spearman correlations around $r_{sp} = 0.7$) between measured and modelled values for both outdoor and indoor static locations. Epidemiological studies (e.g. (12)) have used these fixed site estimates as exposure assessment with the implicit assumption that they reflect personal exposure levels. However, the agreement between measurements and model predictions at static locations does not account for subject movement patterns, and therefore agreement with personal measurements may be lower.

Studies that compared geospatial model predictions with personal measurements are scarce. A study (13) by Frei et al. (2010) found a poor correlation between model predictions and personal 7 days measurements ($r_{sp} = 0.28$) based on a comparison of model predictions by NISMap of RF-EMF levels from fixed site transmitters (FM, TV, Tetrapol, mobile phone base station downlink (hereafter referred to as downlink)) with personal measurements from all far field RF-EMF exposure sources (including FM, TV, Tetrapol, mobile phone downlink, but also mobile phone uplink (hereafter referred to as uplink), DECT, and W-LAN). Martens et al. (2015) (14) compared downlink predictions by NISMap with downlink personal measurements for a 24-h period and found a slightly higher but still modest Spearman correlation ($r_{sp} = 0.36$). These previous results would indicate that there is considerable misclassification in personal RF-EMF exposure levels when approximated by fixed site estimates. However, these previous studies may have suffered from several methodological limitations. First, the measurement devices used in these studies (EME-SPY 120:(15), EME-SPY 121: (14)) were not sensitive enough to detect low field strengths (below 6.63E-03 mW/m²), they underestimate actual RF-EMF levels and may suffer from crosstalk between different frequency bands (16, 17). Recently, improved measurement devices such as EME-SPY 140 and the ExpoM3 have become available. Secondly, the use of more accurate height and antenna input data can improve the accuracy of NISMap model predictions (18).

In this study, we compare NISMap model predictions with personal 48h, at home, at night, and static measurements in the bedroom, using more accurate height and antenna input data and contemporary measurement instruments. We will address two factors that could impact exposure assessment in epidemiological studies: (i) variability in areas with different degrees of urbanisation, as different spatial characteristics (build-up topology) in urban versus rural areas may influence the accuracy of the model predictions; and (ii) the relative contribution of downlink RF-EMF exposure to total far field RF-EMF exposure, and whether this contribution is different for high and low exposed subjects.

2. Method

2.1 Population and sampling strategy

The sampling strategy and flow of participants are displayed in Fig. 1. To recruit participants distributed across a broad exposure range, we used NISMap to estimate RF-EMF downlink levels for 9,563 randomly selected addresses in five towns near Utrecht, the Netherlands (Bunnik, Odijk, Zeist, de Bilt and Bilthoven). Potential subjects (one per household) were approached through postal mail addressed to their household. These households were selected based on geographical spread, variation in urbanisation degree (information about the urbanisation level at postal code level was obtained from the Dutch CBS (Statistics Netherlands)), and a broad variation in exposure range. Based on initial exposure estimation (see model description and model input) we invited potential subjects equally distributed over three categories: < 0.0265 mW/m², 0.0265 - 0.106 mW/m² and > 0.106 mW/m². The thresholds 0.0265 mW/m² (0.1 V/m) and 0.106 mW/m² (0.2 Vm) corresponded with respectively the top 10% and the top 1% of the distribution of modelled (initial) RF-EMF downlink values. Assumed low exposed subjects (<0.0265 mW/m²) were sampled from the same neighbourhoods as higher exposed subjects to ensure maximum comparability (e.g. similar type of residences). No more than two households from each street, and no addresses directly next to each other, could participate, so that sufficient geographical spread was achieved, and

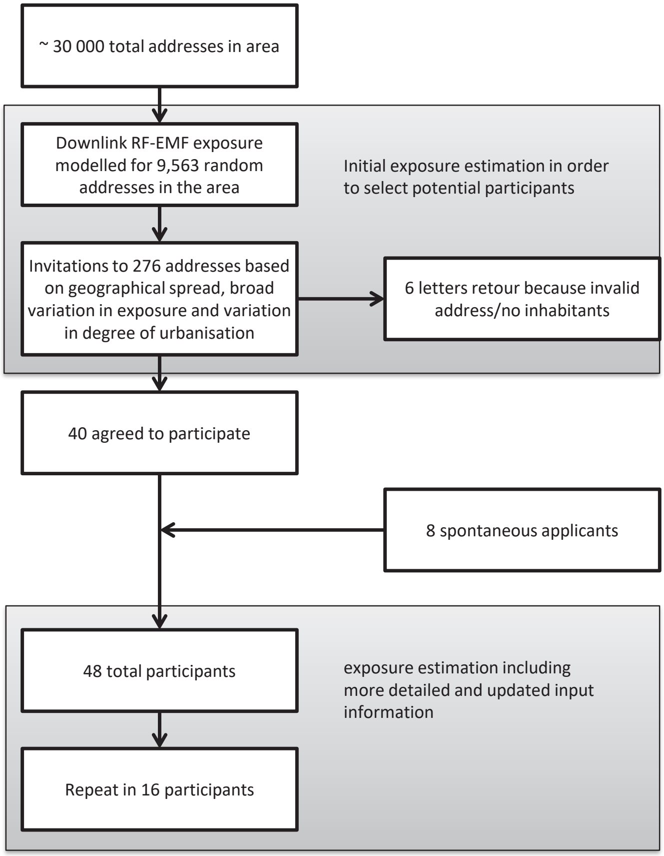

Figure 1. Participant sampling strategy and flow of participants

to avoid correlated errors. Invitation letters were sent in batches of approximately 50 letters each until the desired number of participants was reached. From the 276 invitation letters that were sent, 40 individuals participated, as well as eight spontaneous applicants who were friends or (distant) neighbours from the selected households. All participants signed a written informed consent. Participants were given a 20-euro voucher as an incentive. After completing the first set of measurements, we asked if the participant was willing to take part in a repeated measurement, which 16 participants agreed to. The purpose of these repeated measurements was to assess whether one 48h measurement period is an adequate period to assess long-term personal exposure. All measurements took place between November 2013 and May 2014.

2.2 Model description and model input

We modelled RF-EMF exposure to different downlink frequencies (UMTS, GSM900, GSM1800) from mobile phone base stations in the bedroom of the study participants using a three-dimensional radio wave propagation model (NISMap). We first modelled exposure for 9,563 random selected households out of an approximate 30,000 households in the study area. This allowed the selection of participants over a broad exposure range. For this initial estimation we had no information on the bedroom height, which in previous uncertainty analyses has been shown to be influential (18), and had available only an older list of the presence of communication transmitters. Therefore, we remodelled exposure for all participants with more detailed and updated input data. The required input data and technical details of the model have been described in several previous studies (e.g. (8, 9, 19). Briefly, detailed information on communication transmitters (for initial estimation transmitter data from 2011 and for the final estimation transmitter data from 2013), such as the coordinates, beam direction, and height of the transmitter was obtained from the Dutch Radiocommunications Agency (Agentschap Telecom). The estimated output power of the antennas is based on long-term averages. Coordinates of home addresses were obtained from the Dutch Cadastre in 2012 (BAG, Basisregistraties Adressen en Gebouwen). A 3D representation of all buildings in the Netherlands was constructed by combining data on the building locations and outline from the national BAG building data set with height information from the Netherlands elevation model (Actueel Hoogtebestand Nederland 2, AHN2).

Decrease of RF-EMF levels with distance were calculated using the Double Power Law (20) as previously done by Bürgi et al. (2010) (9) and Beekhuizen et al. (2013, 2014)(10, 11). Building damping values were set equal to Martens et al. (2015) (14) to correct for the attenuation of radio waves by buildings. Damping of roofs was set to 4.5 dB, damping of walls to 3 dB and the inside damping to 0.6 dB/m for all buildings. The bedroom height was used as input for the model, as people generally spend the majority of their time in their bedroom while they are at home. For the initial model estimation to select participants, the bedroom height input was set at 4.5 metres, unless the total building height was lower than 5.0 metres. In that case we used the total building height minus 0.5 metres. To obtain the bedroom height for the final model estimation, we asked subjects the total number of floors in the building and the floor number of their bedroom (where ground level counts as zero). We used the following formula to calculate approximate bedroom height (11):

$$\text{bedroom height} = \frac{\text{building height in meters}}{\text{total number of floors}} * \text{floornumber bedroom} + 1.5 \text{ metres}$$

2.3 Bedroom measurements

Bedroom spot measurements were performed by the researchers at the home addresses of all study participants using a Satimo EME-SPY 140 exposimeter (the detection limit for the downlink frequencies was $6.63 * 10^{-5}$ mW/m^2 (0.005 V/m) sampling every 4 seconds (http://www.eudisa.com/fileadmin/PDFs/industrieloesungen/EMESPY140_EN.pdf). The Satimo EME-SPY 140 measures the RF-electric fields in 14 separate frequency bands ranging from FM (88 – 108 MHz) to WiFi 5G (5150 – 5850 MHz). This measurement device was chosen for the spot measurements in order to compare the results with our previous studies (11) as well as for the possibility to immediately read out the data to check if the measurements were successful. The measurement device was placed on a wooden tripod. We measured for two minutes at seven spots in the room starting in the centre of the room at height 1.10, 1.50 and 1.70 metres, and in all corners of the room at height 1.50 metres with a distance to the centre of approximately 1 metre (conducted in the same manner as e.g. (9)).

2.4 Personal measurements

To determine personal exposure over a period of 48 consecutive hours, the participants carried a small hip bag containing a radiofrequency meter (ExpoM3, sampling frequency set to every 30 seconds) for a period of 48 hours. The ExpoM3 measures the RF-electric fields in 16 separate frequency bands (ranging from FM Radio (88 – 108 MHz) to WiFi 5G (5150 – 5875 MHz). We did not include the LTE uplink and downlink frequencies for calculating total far field RF-EMF exposure (see table 1 for a list of frequencies), as LTE was not yet introduced in our study area at the time of the measurements. The ExpoM

Table 1. Frequency bands from the ExpoM 3 used to calculate total far field RF-EMF exposure

Band name	Frequency range
FM Radio	87.5 – 108 MHz
DVB-T	470 – 790 MHz
GSM900 uplink	880 – 915 MHz
GSM900 downlink	925 – 960 MHz
GSM1800 uplink	1710 – 1785 MHz
GSM1800 downlink	1805 – 1880 MHz
DECT	1880 – 1900 MHz
UMTS uplink	1920 – 1980 MHz
UMTS downlink	2110 – 2170 MHz
ISM 2.4 GHz	2400 – 2485 MHz
WiMax 3.5 GHz	3400 – 3600 MHz
ISM 5.8 GHz / U-NII 1-2e	5150 – 5875 MHz

measurement device was chosen for personal measurements for its small size and low weight, as well as long battery life since we aimed for a 48h measurement period. The lower detection limits of the ExpoM3 radiofrequency meter for the downlink frequencies were: UMTS downlink: $2.39 * 10^{-5}$ mW/m² or (0.003 V/m), GSM900 downlink: 6.63 $* 10^{-5}$ mW/m² or (0.005 V/m) and GSM1800 downlink: $6.63 * 10^{-5}$ mW/m² (or 0.005 V/m). Participants were asked to continue their daily activities as usual. During sleep, participants were asked to place the cotton bag containing the device on a bedside table at a minimum distance of 30 centimetres from the wall. We asked participants to keep a diary in which they specified at what times they left and entered their home. The diary was also used to register any time the participant did not carry the bag with the measurement device (for example swimming, sports or forgetting to wear the bag) as well as to register any incidents such as dropping the bag by accident.

2.5 Urbanisation

To get a measure of the degree of urbanisation, we used the address density for each postal code, based on publicly available data from the Central Bureau of Statistics (2010) (five categories: < 500, 501-1000, 1001-1500, 1501-2500 and - >2500 addresses per km²). We dichotomized this variable because of few observations in some of the categories to two categories: low urbanisation, 0-1500 addresses per km²; and high urbanisation, >1500 addresses per km².

2.6 Data analysis

In a few instances, short time slots of the 48h measurement periods were removed from the data because the participant reported in the diary not having carried the measurement device for reasons other than night-time (for example because the participant went running outside and it was inconvenient to carry the measurement device). In total, this amounted to 17.5h summed over six participants, which was less than 1% of the total (2076h) sampled hours.

Measurements below the detection limit were set at the detection limit (for the EME-SPY spot measurements in the bedroom: 0% of the GSM900 DL, 30% of the GSM1800, and 15% of the UMTS DL. For the ExpoM3, 48h personal measurements: 2% of the GSM900 DL, 12% of the GSM1800, and 20% of the UMTS).

We computed the total downlink exposure for each subject by summing the mean RF-EMF levels of the GSM 900 downlink, GSM 1800 downlink and UMTS downlink frequencies (in mW/m²) for the following periods: the overall 48h period, the time spent at home as reported in the diary, and assumed night-time between 0:00 and 08:00 AM. Of 21 participants the actual night-time (mean duration: 16.4h, start time: 23:32, and end time: 07:41) was known and we used this data in a sensitivity analysis. Furthermore, we assessed the agreement between the initial and final model estimation to evaluate the method of participant selection. In addition, we evaluated the repeated 48h sampling scheme for personal measurements by comparing initial and repeated 48h measurements using the intraclass correlation and Spearman (r_{Sp})coefficients.

We computed several indicators to determine the accuracy of the NISMap model predictions: mean modelled and measured values, ratio (mean modelled value divided by the mean measured value), mean difference between modelled and measured values (modelled - measured), mean relative difference (mean difference divided by the average of measured and modelled values), precision (standard deviation of differences between modelled and measured values), coefficient of variation (ratio of the standard deviation to the mean) and Spearman rank correlation between modelled and measured values. We compared differences in the association between model predictions and measurements between areas with high and low urbanisation.

We compared the contribution of each frequency to the total far field RF-EMF 48h exposure for all participants and for participants with downlink exposure on or below the median, above the median. Analyses were carried out using the statistical programme R (3.1.0) and SAS 9.2.

3. Results

3.1 Descriptives

One participant had to be excluded from the analyses due to failure of the ExpoM3. Failure of the ExpoM3 also occurred in two other instances, but in those cases at least one set of measurements (first or repeated measurement set) was successful. Therefore, we analysed data for 47 unique participants and 14 repeated measurements resulting in total 61 observations.

Our study population consisted of 26 male subjects and 21 female subjects between the ages of 21 and 80. Less than half of the participants lived in urban areas (N = 21; 45%) while the other participants lived in more rural areas (n = 26; 55%). The mean measured duration with the ExpoM3 for all participants was 43.8 hours, including night-time and time spent outside the home and excluding day-time periods not carrying the device. On average, participants were at home for 34.2 hours (78%). In a sensitivity analysis (n=21) we compared the measurement values for actual reported bedtime and the assumed night-time, and these were similar (reported bedtime: mean 0.151 mW/m^2 (SD

0.402), assumed night-time: mean 0.151 mW/m² (SD 0.404). We therefore conducted all analyses using the assumed bedtime allowing the use of the full set of 47 participants.

3.2 Description of initial model estimation

The mean initial exposure for 9,563 random addresses in the area estimated by NISMap was 0.010 mW/m² (SD 0.024) for all addresses, 0.078 mW/m² (SD 0.062) for the 40 participants in the study that were selected based on the initial estimation. The mean final NISMap model estimation for these 40 participants was 0.159 mW/m² (SD 0.238), and the correlation between the initial and the final estimation was r_{Sp}=0.40. Including the spontaneous applicants resulted in an average exposure of 0.140 mW/m² (SD 0.225).

3.3 Inter- and intra-individual variability in RF-EMF measurements

We assessed the variability for the first and repeat 48h measurements available for 14 participants. There was more inter-individual (between persons) variation than intra-individual (between the first and repeat sets of measurements) variation, as reflected in a high intraclass correlation (0.81) and Spearman correlation (r_{Sp}=0.76). Subsequent analyses are therefore based on the first successful 48h measurement period of all participants.

3.4 Accuracy of the model predictions

Table 2 shows the distribution of modelled and measured 48h downlink RF-EMF values for all 47 participants. Table 3 shows the accuracy of the model predictions for the first measurement of all 47 participants. The mean modelled value for the 48h overall period was 0.140 mW/m², the mean measured value was 0.091 mW/m². The mean measured value from the spot measurements in the bedroom was 0.292 mW/m². We found a Spearman correlation of r_{Sp}= 0.47 between modelled and measured values for the 48h overall period, and r_{Sp}=0.54 between model predictions and spot measurements in the bedroom. In figure 2 we show two Bland-Altman plots (21) for the absolute (Figure 2A) and the relative differences (Figure 2B) between the NISMap model predictions and the 48h personal measurements. We more often observe overestimation than underestima-

Table 2. Distribution of modelled and measured values of RF-EMF far field downlink (mW/m²) for all 47 participants

	Min	25% quantile	median	75% quantile	max
modelled	0.000	0.025	0.066	0.141	1.210
Measured 48h	0.002	0.010	0.027	0.051	1.526
Measured at home	0.001	0.005	0.012	0.050	1.547
Measured at night	0.000	0.004	0.011	0.057	1.829

tion of RF-EMF, and the degree of overestimation increases for higher absolute values, but not for relative values. There are no consistent differences in relative prediction accuracy (Figure 2, Table 4 (r_{Sp})) for addresses in high versus low urbanized areas. However, measured values are higher in low urbanized areas, while modelled values are similar in high and low urbanized areas, resulting in different modelled/measured ratios.

3.5 Downlink contribution to total far field RF-EMF

On average, downlink exposure contributed for 64% to total far field RF-EMF exposure for the 48h period. When the contribution is assessed separately for subjects with a downlink exposure below and above median, we find that downlink contributed respectively 18% and 76% to the total far field RF-EMF exposure.

4. Discussion

4.1 Interpretation of findings

In this study, we expanded on previous studies to assess the validity of using NISMap model predictions at the home address as a proxy for personal downlink RF-EMF exposure from mobile phone base stations in epidemiological studies. Compared to previous studies (9, 14), we included more high exposed subjects and used improved model input data, as well as contemporary measurement devices. Our results showed that participants can be meaningfully ranked by modelled exposure at the home address irrespective of the degree of urbanisation, and that RF-EMF from mobile phone base stations can be a major source of total RF-EMF exposure for a portion of the population with high downlink exposure.

A similar measurement study with data from 2009/2010 reported a Spearman correlation of r_{Sp}=0.36 between model predictions and 24h personal measurements (14). The current study indicated better agreement (r_{Sp}= 0.47) between model predictions and personal measurements, possible owing to improved measurement devices (EME-SPY 140 vs. EME-SPY 120) and better model input data, mainly improved height estimation, and improved transmitter data. Beekhuizen et al., (2014) (11) collected spot measurements in the bedroom for 30 households and found a Spearman correlation of r_{Sp}= 0.60 with model predictions using NISMap. In our study, we found a similar value (r_{Sp}= 0.54). Since the spot measurements in the bedroom corresponded most closely with the modelled location by NISMap, we expected better agreement between these spot measurements and the model predictions than with personal 48h measurements. The difference in correlation between 'spot measurements–model prediction' and 'personal 48h measurement–model prediction' can be interpreted as the loss in predic-

Table 3. Comparison of downlink RF-EMF (mW/m²) model predictions with personal 48h, time spent at home, and at night measurements, and with spot measurements in the bedroom

	Personal 48h (ExpoM3)	At home (ExpoM3)	At night 0:00-08:00 (ExpoM3)	Spot measurements bedroom (EME-SPY 140)
mean measured	0.091	0.083	0.090	0.292
mean modelled	0.140	0.140	0.140	0.140
Ratio modelled/measured	1.532	1.691	1.557	0.478
mean difference (modelled-measured)	0.048	0.057	0.050	-0.152
mean relative difference	0.30	0.60	0.61	0.41
Precision	0.17	0.17	0.20	0.82
Coefficient of variation	2.60	2.90	3.01	3.66
r_{Sp} correlation between measured and modelled	0.47	0.49	0.51	0.54

Table 4. Mean RF-EMF downlink exposure (mW/m²) and Spearman correlations with modelled exposure by urbanisation*

	High urbanity (n=21)			Low urbanity (n=26)		
	Mean	r_{Sp}	Ratio modelled/ measured	Mean	r_{Sp}	Ratio modelled/ measured
Modelled	0.152			0.130		
Measured						
48h period	0.068	0.38	2.22	0.110	0.55	1.18
At home	0.069	0.52	2.21	0.094	0.46	1.38
At night	0.060	0.46	2.52	0.113	0.59	1.14
Spot measurements in bedroom	0.168	0.55	0.91	0.393	0.50	0.33

*high urbanisation: >1500 addresses per km², low urbanisation: <=1500 addresses per km²

tion accuracy due to personal movement patterns. In our study, the loss in accuracy (0.54-0.47) seems minimal. The extent of the loss in prediction accuracy is influenced by the amount of time participants spend at home/in the bedroom, and by activities/ locations. Our study population spent somewhat more time at home (78%) than in other environmental studies (65-70%, e.g. (14, 22)), which may have resulted in a slightly optimistic estimate of the loss in prediction accuracy.

We were especially interested in knowing if the prediction accuracy differed by urbanisation degree. If this would be the case, this could bias exposure estimations and as a consequence, might bias epidemiological exposure-response analyses especially if the health effect of interest is also associated with level of urbanisation. Earlier validation studies by Beekhuizen et al. focused on highly urbanized areas, with more complicated spatial characteristics and potentially less accurate model estimation than in low urbanized areas. Our results did not indicate clear differences in correlation (Figure 2, Table 4). However, the modelled/measured ratios were lower in less urbanized areas, and urbanisation degree should remain a point of attention in exposure assessment.

Previous studies reported that the contribution of RF-EMF exposure from mobile phone base stations to total far field RF-EMF exposure differs across countries and activities but is generally low (23, 24). Neubauer et al., (2007) (7) did not recommend epidemiological studies on RF-EMF exposure to mobile phone base stations alone, due to uncertainty in exposure assessment and low contribution to overall RF-EMF exposure in general. Our results show that this contribution differs depending on the level of exposure to RF-EMF from mobile phone base stations. For participants in our study with exposure from mobile phone base stations above the median, the contribution to total far field RF-EMF exposure was 76%, compared to 18% for participants with lower exposure.

4.2 Strengths and limitations

Strengths of this study were the accurate input data for the NISMap model predictions and the contemporary measurement devices used to measure RF-EMF fields. In contrast to previous studies (11, 14, 13), we did not focus on spot measurements or on personal measurements, but did both type of measurements, enabling us to evaluate the impact of personal movement patterns on prediction accuracy. Previous RF-EMF personal measurement studies differed in the length of the measurement period ((15):1 week, (14): 24 hours). Large temporal variation in personal exposure patterns could mean that longer measurement periods or repeated measurements would be necessary to get an indication of the typical long-term exposure of an individual. We found a high intraclass correlation (0.81) between repeated measurements, indicating that one measurement period of 48 hours is adequate to assess long-term personal exposure.

A limitation of this study arose from using different measurement devices for spot measurements in the bedroom (EME-SPY 140) and personal measurements (ExpoM3), which may have influenced the comparison between spot measurements and personal measurements. The ratio of modelled to measured values were different for the measurements with the ExpoM3 and the EME-SPY 140 device. However, limited side-by-side testing of the two devices (results not presented) showed no consistent differences between values of the two measurement devices and all measurement devices were calibrated both before and after the measurement period. Like model predictions, measurements have their own limitations, and are not a perfect 'golden standard' (16, 17). Another limitation of this study was the lack of information regarding mobile and DECT phone use. Gaining information about phone use would require more detailed activity diaries, which can be bothersome for participants and lead to selective dropout. Phone use is a source of near field RF-EMF exposure (the uplink and DECT frequencies), for which there can be large differences in measurement values depending on small differences in distance. Measurement devices such as the ExpoM3 can therefore not give a reliable indication of full-body near field exposure, and the measurement values in the uplink bands of our measurement values (data not presented here) are a mix of both near field exposure (own phone use) and far field exposure (phone use by other people in the area). Therefore, and given our study aim, we focused on downlink frequencies.

We oversampled high exposed subjects to obtain subjects across a broad range of exposure, using an initial model estimation with incomplete input data (less accurate height input and transmitter data). A disadvantage of this selection method is that the results of this study are not representative for the general population. We selected all participants from the same neighbourhoods as participants living at addresses with a high exposure estimate based on the initial estimation. As a consequence, we have selected neighbourhoods with high exposure contrasts, which may reflect spatial characteristics of these neighbourhoods such as large variation in building heights. Since estimation of exposure with a 3D geospatial model may be more difficult in such areas than in areas with less spatial variation, we may have slightly underestimated the ability of NISMap to classify subjects as high or low exposed.

4.3 Conclusion

Findings of previous measurement studies suggested that the agreement between model estimations of downlink RF-EMF from mobile phone base stations at the home address and personal measurements was substantially lower than the agreement with measurements at a static location. In our study, we found that the loss in prediction accuracy resulting from movement patterns and specifically, the time spent at locations other than the home address, is limited. Although misclassification is present, it is possible to meaningfully rank participants on modelled downlink exposure and to identify relatively high exposed individuals, both for low and high degree of urbanisation. The contribution of exposure from mobile phone base stations to total far field RF-EMF exposure can be substantial for subjects with a high exposure. Large epidemiological studies regarding health effects of RF-EMF from mobile phone base stations are now feasible, as limited individual input data is required owing to the availability of an adequate prediction model.

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Modeled and perceived RF-EMF exposure from mobile phone base stations in relation to symptom reporting

Somatic symptom reports in the general population: Application of a bi-factor model to the analysis of change

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ABSTRACT

Objective: To investigate the latent structure of somatic symptom reports in the general population with a bi-factor model and apply the structure to the analysis of change in reported symptoms after the emergence of an uncertain environmental health risk.

Methods: Somatic symptoms were assessed in two general population environmental health cohorts (AMIGO, n = 14,829 & POWER, n = 951) using the somatization scale of the four-dimensional symptom questionnaire (4DSQ-S). Exploratory bi-factor analysis was used to determine the factor structure in the AMIGO cohort. Multi-group and longitudinal models were applied to assess measurement invariance. For a subsample of residents living close to a newly introduced power line (n = 224), we compared a uni- and multidimensional method for the analysis of change in reported symptoms after the power line was put into operation.

Results: We found a good fit (RMSEA = 0.03, CFI = 0.98) for a bi-factor model with one general and three symptom specific factors (musculoskeletal, gastrointestinal, cardio-pulmonary). The latent structure was found to be invariant between cohorts and over time. A significant increase ($p < .05$) was found only for musculoskeletal and gastrointestinal symptoms after the power line was put into operation.

Conclusions: In our study, we found that a bi-factor structure of somatic symptoms reports was equivalent between cohorts and over time. Our findings suggest that taking this structure into account can lead to a more informative interpretation of a change in symptom reports compared to a unidimensional approach.

1. INTRODUCTION

The experience of non-specific somatic symptoms such as headaches or back pain has negative effects on daily functioning in a considerable proportion of the general population, and is a major cause of health care utilization (1–3). These experiences are typically assessed with self-report questionnaires (4) and are frequently used in varying research disciplines such as psychosomatic medicine [e.g. 5] or environmental health [e.g. 6,7]. In most studies the total symptom score is analyzed and/or the individual symptoms separately. Neither approach reflects the multifactorial origin of reporting somatic symptoms (8, 9).

Self-report symptom questionnaires such as the PHQ-15 (10) or the SCL-90 SOM (11) were designed to measure the experience of distressing somatic symptoms. A high score (clinical cut-off scores are generally provided) is interpreted as an indication of somatization. Although these questionnaires were designed to measure one underlying construct (i.e. somatization), there is evidence for the latent structure to be multi- rather than unidimensional (12–15). This is due to the existence of specific symptom patterns, such as symptoms pertaining to musculoskeletal or gastrointestinal complaints. A wide range of influences can lead to higher scores on symptoms from a specific symptom group (e.g. infections, diseases, and psychosocial distress) while scores on other domains are less affected. It is therefore plausible that additional variance in reported symptoms is explained by symptom specific factors. The bi-factor model separates the general variance of scores on all symptoms (i.e. general factor, representing a general tendency to report symptoms), from the unique variance of scores relating to specific symptom groups (i.e. specific factors). This model allows studying both components of somatic symptom reporting simultaneously.

So far, only a few studies (16–18) have applied a bi-factor model to data gathered with symptom questionnaires. These studies showed that specific factors explain unique variance over and above the common variance in symptom reporting explained by a general factor. In addition the bi-factor model has been shown to provide a better fit than alternative factor models. However, the evidence gathered so far is limited and mainly based on two cross-sectional clinical samples using two different symptom questionnaires. There may be differences in the underlying structure between populations and symptom questionnaires which could impact application to health effect studies.

In order to compare symptom scores on underlying constructs between different populations and over time, measurement invariance (MI) must be established (19). MI refers to the underlying factor structure being equivalent across samples and over time.

Changes in the underlying factor structure complicate the interpretation of differences in symptom scores. When the structure is not invariant a score difference could reflect a change in the score on the underlying latent construct, or reflect a change in the construct itself. If MI can be established, there may be useful practical applications of the bi-factor model to intervention studies using somatic symptom reports as an outcome. One could assess the effect of an intervention or exposure on general symptom reporting (i.e. over and above reporting symptoms from specific symptom groups), as well as on symptom specific factors (i.e. over and above general symptom reporting). A potential benefit of a bi-factor model is the greater conceptual clarity provided by a separation between general and specific variance (20).

The aim of the present study is threefold. First, we aim to test the structural validity of a bi-factor model for the somatization scale of the 4DSQ [4DSQ-S, 21] in a large general population sample. Structural validity of this subscale has not been investigated before. Second, we assess MI of the resulting latent structure by comparing the structure between two different general population samples, as well as across time in one sample. Third and last, we apply a bi-factor structure to analyze change in symptom reports after the emergence of an uncertain environmental health risk. In previous work we found a greater increase in overall reported somatic symptoms after a new power line was put into operation for residents living close by, compared to a control group of residents living farther away (22). We extend those findings by evaluating the change in reported somatic symptoms in line with the underlying latent structure of the 4DSQ-S.

2. METHODS

2.1. Participants

Participants were members of the adult general population in the Netherlands enrolled in two different cohorts. The first cohort (AMIGO) was set up to study environmental and occupational determinants of diseases and symptoms [see 23 for a full description]. The AMIGO cohort at baseline consisted of 14,829 subjects of which 50.2% men. The mean age of the AMIGO participants was 51 years (SD = 9). The second cohort (POWER) was set up to study health responses to the introduction of a new high-voltage power line [see 24 for a full description]. At baseline the POWER cohort consisted of 951 subjects of which 46% men. Mean age of the participants was 52 years (SD = 13). The longitudinal models to assess measurement invariance were based on a total of 1241 subjects. This number is higher than the number of participants at baseline, because new subjects were enrolled at T2 (22). For the analysis of change we focused on the group of residents within 300 meter of the new high voltage power line (n=224), as we established in previous work that only this group experienced more symptoms after the line was put into operation (22). The overall response rate to the baseline questionnaires was similar in both cohorts (AMIGO: 16%, POWER: 19%).

2.2. Procedures

In both cohorts, invitations were sent through postal mail. Both studies were presented to participants as longitudinal environmental health studies, which consisted of filling out questionnaires by one adult per household about health and the environment. To reduce the chance of response bias, there was no mentioning of power lines in the POWER cohort invitation letter.

The AMIGO cohort subjects (31-65 years old) were recruited using a national information network of general practitioners established at the Netherlands Institute for Health Services Research (NIVEL), called NIVEL Primary Care Database. Participants were invited between April 2011 and July 2012. For the POWER cohort one member older than 18 of each household within 500 meters of the planned construction of a new power line (n = 2379) was invited to participate, as well as a random stratified sample of households within 500-2000 meters (n = 2382). Data was collected before the power line was put into operation, starting in June 2012 (T1), 5 months later (T2), and after the power line was put into operation, 12 months (T3) and 18 months (T4) after the baseline measurement (T1). The study protocols of both studies were approved by the Medical Ethics Committee of the research boards of the involved institutes, and all participants participated voluntarily with informed consent.

2.3. Measures

Somatic symptoms

In both cohorts the somatization scale of the 4DSQ (21) was used to assess self-reported somatic symptoms. The 4DSQ consists of 4 scales measuring distress, depression, anxiety and somatization, but only the somatization scale was administered in our study samples. The somatization scale (4DSQ-S) consists of 16 non-specific somatic symptoms (e.g. headaches, low back pain, and dizziness) commonly reported in general practices (see Figure 1 for a list of all symptoms). For each symptom, participants indicated whether they were bothered by it during the previous week on a 5-point scale (ranging from no, through to constantly). The scores were trichotomized before analysis (no = 0; sometimes = 1, regularly/often/constantly = 2) (21).

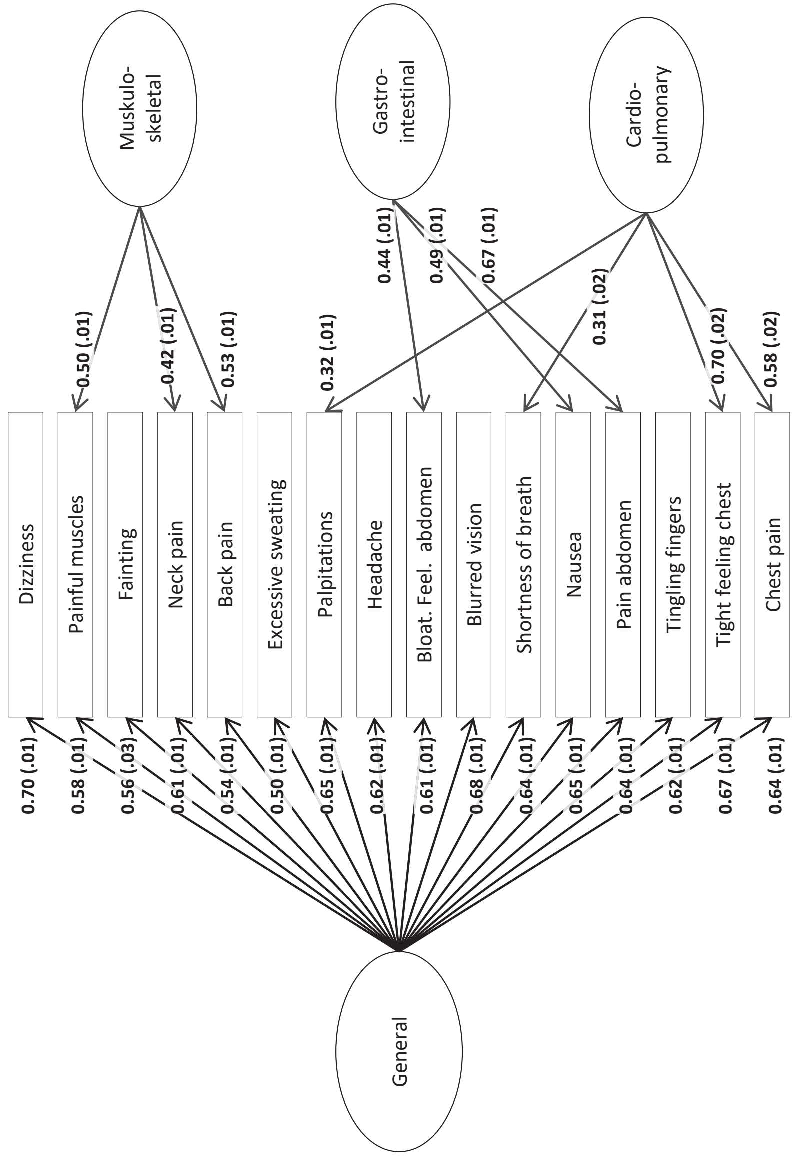

Figure 1. AMIGO confirmatory baseline bi-factor model with standardized factor loadings and standard errors.

2.4. Statistical analyses

To answer the first research question regarding the underlying latent structure of the 4DSQ-S we conducted a categorical exploratory bi-factor analysis on the AMIGO baseline data with Bi-Geomin rotation (22) and WLSMV estimation. Two (1 general, 1 specific factor) up to six (1 general, 5 specific factors) factor solutions were considered and one bi-factor specification was selected for a confirmatory analysis, based on the theoretical interpretation of the models as well as the statistical fit. We assigned items to a factor only if the factor loading for that item on that factor was greater than 0.30. The variances of the common factors were identified by fixing the loading of the first item to one. Root mean square error of approximation (RMSEA) and comparative fit index (CFI) were used to assess model fit. For RMSEA, models with values ≤ 0.06 had acceptable fit and for CFI values ≥ 0.95 had acceptable fit (26).

To answer the second research question regarding MI of the 4DSQ-S we fitted a multi-group model where we increasingly constrained more parameters to be equal across the baseline AMIGO and POWER cohort samples to assess invariance (19, 27). The following models were tested consecutively: configural invariance (factor loadings freely estimated and thresholds constrained), loading invariance (factor loadings and thresholds constrained), and residual invariance (factor loadings, thresholds and residual variance constrained). We compared the models using the criteria suggested by Chen et al. (28) to establish MI: a decrease in CFI of ≥ 0.01, and an increase in RMSEA of ≥ 0.015 were interpreted as an unacceptable decrease in model fit (i.e. indicating absence of MI).

To test whether the measurement model was invariant across time within the full POWER cohort we used similar procedures [see 29]. In addition to cross-sectional orthogonal constraints between the general and specific factors and constraints necessary for identification, we added orthogonal constraints to the longitudinal relations between latent factors (30). Residuals of the same indicators over time were allowed to correlate. Comparison of the models and assessment of model fit was similar to the multi-group models.

To answer the third and final research question regarding the analysis of change in reported somatic symptoms, we applied linear mixed models with an unstructured residual covariance structure to the data gathered from participants in the POWER cohort living within 0-300 meters of the new power line (n = 224). Sum scores were calculated for the specific symptom factors identified in the bi-factor analysis of the 4DSQ-S, as well as the total sum score as indication of the general factor. Time was entered as categorical predictor (T2, T3, and T4) with T1 as reference category. We compared two different ways to analyze change in reported somatic symptoms. First, the standard approach where we assessed the effects of time (i.e. change from baseline) on the specific and total sum scores. Second, a bi-factor approach, where we adjusted the effects of time on specific symptom scores for the total sum score (minus overlapping items). This analysis indicates to what extent a change in reports from specific symptom groups was confounded by a general symptom reporting pattern. For the mixed model with the total sum score as outcome, we adjusted the effect of time for scores on the specific symptom groups. This analysis indicates to what extent a change in overall symptom reporting was confounded by specific symptom patterns.

SPSS version 20 was used for the mixed models analyses; Mplus version 7.2 was used for all other analyses.

3. RESULTS

3.1. Latent structure of the 4DSQ-S

Information about all symptoms was missing for 330 (2%) subjects in the AMIGO cohort, and for 11 (1%) in the baseline POWER cohort. These subjects were not included in further analyses. The exploratory bi-factor analyses indicated that a model with one general and three specific factors provided a good fit (RMSEA = 0.027, CFI = 0.992) to the AMGIO baseline data, and was most readily interpretable. We named the specific factors musculoskeletal (muscle pain, neck pain, back pain), gastrointestinal (bloated feeling in abdomen, nausea, pain in stomach) and cardiopulmonary (palpitations, shortness of breath, tight feeling in chest, pain in chest). Fit indices of the confirmatory bi-factor model in the baseline AMIGO (RMSEA = 0.032, CFI = 0.984) and POWER cohort (RMSEA = 0.029, CFI = 0.985) indicated that the selected bi-factor model fitted well to the data from both cohorts. Figure 1 presents the confirmatory AMIGO baseline model with standardized factor loadings for the 4DSQ-S items on the general and symptom specific factors.

3.2. Measurement invariance of the bi-factor model

Table 1 shows the fit statistics for the measurement invariance models. For both the multi-group and longitudinal models, the fit indices indicated a good fit to the data (i.e. RMSEA ≤ 0.06 and CFI ≥ 0.95). If the RMSEA and CFI values do not deteriorate in the more constrained models (i.e. the loading and residual invariance models), this is indicative of measurement invariance. As can be seen in Table 1, there was no decrease in fit for the more restricted models in the multi-group and longitudinal comparisons. The

Table 1. Model fit indices for the measurement invariance models.

Model	n	Chi-square	d.f.	*p*-Value	CFI	RMSEA	RMSEA 90%-CI
Multi-group baseline (AMIGO & POWER)							
Configural invariance[a]	15439	1636.383	200	< 0.001	0.983	0.031	0.029 – 0.032
Loading invariance[b]	15439	1421.149	222	< 0.001	0.986	0.026	0.025 – 0.028
Residual invariance[c]	15439	1253.197	238	< 0.001	0.988	0.024	0.022 – 0.025
Longitudinal[d] (POWER)							
Configural invariance[a]	1241	1920.475	1589	< 0.001	0.987	0.013	0.011 – 0.015
Loading invariance[b]	1241	1971.465	1652	< 0.001	0.987	0.012	0.010 – 0.015
Residual invariance[c]	1241	1960.503	1697	< 0.001	0.989	0.011	0.009 – 0.013

[a] factor loadings freely estimated and thresholds constrained.
[b] factor loadings and thresholds constrained.
[c] factor loadings, thresholds and residual variance constrained.
[d] The item assessing 'fainting' was removed from the longitudinal models due to counts of 0 in the higher categories (sometimes = 1, regularly/often/constantly = 2) at some time-points.

differences are well below the suggested cut-off points for establishing MI (a decrease in CFI of ≥ 0.01, and an increase in RMSEA of ≥ 0.015 (25)).

3.3. Change in somatic symptom patterns

Table 2 displays the parameter estimates for the change from baseline for the general and symptom specific scores in participants living close to the newly introduced power line. The mean scores at baseline (T1) were 4.02 (SD = 3.81) for the total sum score of somatic complaints, 1.53 (SD = 1.55) for musculoskeletal, 0.63 (SD = 1.01) for gastro-intestinal, and 0.42 (SD = 0.87) for cardiopulmonary complaints. After the new power line was put into operation we found an increase in overall symptom reports (on the total sum score) from baseline (previously reported in 22). When these estimates were adjusted for scores on the symptom specific factors, in line with a bi-factor model, we no longer found a significant change from baseline in the total score. This suggests that the change we found using a sum score of the total scale was mainly due to change in symptom specific factors. This was confirmed in the mixed models for the symptom specific factors. When we inspected the estimates of the specific symptom scores, a significant increase from baseline was seen for musculoskeletal symptoms at T2, T3 and T4, and for gastrointestinal symptoms at T3. When adjusting for a general symptom reporting pattern, only the change at T4 for musculoskeletal and T3 for gastrointestinal symptoms remained significant.

Table 2. Longitudinal development of general and specific somatic complaints in participants living close (0-300m, n = 224) to a newly introduced power line.

	Beta estimates (95% CI)		
	T2[a]	T3[a]	T4[a]
Somatic complaints			
Total sum score (0-32)	.33 (-.26, .92)	.80 (.23, 1.38)**	.85 (.21, 1.48)**
Adjusted for specific symptoms[b]	-.04 (-.29, .22)	-.09 (-.33, .15)	-.07 (-.31, .18)
Musculoskeletal complaints			
Specific sum score (0-6)	.24 (.02, .46)*	.30 (.03, .57)*	.51 (.25, .76)**
Adjusted for general symptoms[c]	.20 (-.02, .42)	.19 (-.07, .44)	.44 (.19, .68)**
Gastrointestinal complaints			
Specific sum score (0-6)	.10 (-.10, .30)	.29 (.11, .47)**	.11 (-.07, .28)
Adjusted for general symptoms[c]	.08 (-.10, .25)	.22 (.05, .38)*	.01 (-.15, .17)
Cardiopulmonary complaints			
Specific sum score (0-8)	-.01 (-.16, .13)	.07 (-.07, .21)	.09 (-.10, .28)
Adjusted for general symptoms[c]	-.05 (-.19, .09)	.00 (-.14, .14)	.02 (-.16, .19)

* $p < .05$
** $p < .01$
[a] T1 (10 months *before* power line was put into operation) is reference category. T2 = 5 months *before* the line was put into operation, T3 = 2 months *after* the line was put into operation, T4 = 7 months *after* the line was put into operation.
[b] Estimates adjusted for the sum scores of the symptom specific factors (i.e. musculoskeletal, gastrointestinal and cardiopulmonary).
[c] Estimates adjusted for the total sum score minus overlapping items.

4. DISCUSSION

This study applied a multidimensional approach to the analysis of somatic symptom reports in a general population. We found that:

1. A bi-factor model with one general and three specific factors provided a good fit to symptom data from two large general population samples, providing further evidence for a multidimensional latent structure of somatic symptom reports in the general population.
2. The bi-factor structure was stable when measurement invariance was evaluated across two large general population samples, and over time in one sample.
3. Application of the bi-factor structure to a general population sample showed that the longitudinal course of symptom reports differed for the different symptom patterns after emergence of an uncertain environmental health risk.

Previous studies used unidimensional methods to analyze effects of interventions or environmental exposures on symptoms see (31) for an overview. The application of bi-factor models to somatic symptom reports has so far been rare. In two cross-sectional samples a good fit was found for a bi-factor model applied to two different somatic symptom questionnaires; the MMPI-2-RF-RC1 (17) and the frequently used PHQ-15 (16). Both studies found a bi-factor structure with a general factor and a number of specific symptom factors (specific factors found in (16): pain, gastroenterological, cardiopulmonary, fatigue; and in (17): gastrointestinal, head pain, neurological). Although there are some differences, the overall factor structure in these studies is similar to our findings. Differences may be explained by differences in specific symptoms included in the used questionnaires (e.g. no fatigue symptoms in 4DSQ-S).

Our study found that symptom patterns can be affected differently by the emergence of an uncertain environmental health risk. Using a total sum score we previously reported an effect of the introduction of a power line on somatic symptom reports (22). In the present study, we found that the introduction of a new power line was uniquely associated with reporting more musculoskeletal and gastrointestinal somatic complaints when accounting for the general factor. This finding illustrates the relevance of acknowledging the underlying bi-factor structure when studying the mechanisms and determinants of a change in symptom reports. A total sum score of somatic complaints does not reflect just one source of variation which blurs the interpretation of a change if one does not take into account the other known sources (i.e. symptom specific factors). This could particularly be problematic when the changes over time in these sources of variation are in opposite directions. As a result one may develop inappropriate theories to explain the research findings, or implement ineffective intervention strategies (32).

More research into determinants of change in symptom scores on the general and symptom specific factors is needed. Both the general and specific factors may reflect influences of diseases, environmental factors and psychosomatic mechanisms. Findings of Witthoft and colleagues (16) suggest that the general as well as certain specific factors are associated with functional somatic syndromes (e.g. irritable bowel syndrome). They hypothesize that where symptom specific factors might reflect temporary (environmental) influences, the general factor could reflect a disposition relevant for perpetuation of symptom experiences. This might explain the absence of an effect of time on the general factor in the POWER cohort. Any (temporary) intervention or illness may be more likely to affect symptom specific factors, which, if combined with a higher score on the general factor, could be perpetuated and lead to chronic health problems.

There are some limitations to the interpretation of our findings. First, we used a regression based method to study the longitudinal course for each symptom pattern. The assumption in all regression based methods that a construct is measured without error is untenable. Hence, it may be better to investigate change on the different factors within a structural equation model (e.g. latent growth curve model). However, this method requires a large sample size due to the computational complexity of the model. Our experimental group (the subgroup of the POWER cohort living within 300 meters from the new power line (n=224)) was too small to estimate such a model. The current method has the advantage of reduced complexity, but cannot perfectly separate general and specific variance within each item. This is disadvantageous when assessing effects on the general factor over and above effects on specific symptom patterns. The overlap in items leads to overcorrection when including all specific symptom patterns as a covariate, and therefore to less power to demonstrate the unique effect on the general factor.

Second, we used a single symptom questionnaire to address our research questions (i.e. 4DSQ-S). Although this questionnaire represents the major symptom specific groups identified in a review of somatic symptom questionnaires (Zijlema et al., 2013), one might find a different latent structure when other symptoms are probed. To improve the analysis of symptoms in health effect studies, it is important to use a symptom questionnaire which covers all potentially relevant symptom groups (see (33)).

Third and last, we did not investigate whether alternative models such as a hierarchical or correlated factor model would lead to different conclusions regarding change over time. Hierarchical or correlated group factor models are the most likely candidates as these are also multidimensional (34). A disadvantage of the correlated factor model is that it does not explicitly represent a general tendency to report symptoms (general factor). The hierarchical model specifies that there is no direct relationship between the items and the general construct, instead this relationship is mediated by the specific factors (35). We prefer the bi-factor model for our study because of the conceptual differences between the two models. The bi-factor model specifies the specific factors as orthogonal from the general factor. Because of this representation it is possible to study whether symptom scores are affected differently over time for the general and the specific factors.

Strengths of our study are the large sample size to assess the latent structure of symptom reports as well as the extensive assessment of measurement invariance, and its application to the analysis of change with an ecologically valid example. The importance of measurement invariance as a prerequisite to interpret scores on a questionnaire has been widely acknowledged [e.g. 19,29,35], but rarely addressed for the use of symptom questionnaires. By establishing invariance of the bi-factor model for the 4DSQ-S in a general population we found support to study symptom scores based on the underlying constructs over time and to compare scores between different general population samples.

In conclusion, we demonstrated the potential use of applying the bi-factor model in an analysis of change in reported symptoms, using the example of an emerging uncertain environmental health risk. Our findings have implications for the analysis and interpretation of symptom checklists in psychosomatic and (environmental) health research. Application of the bi-factor structure can lead to a more informative interpretation of changes in somatic symptom reporting, as it allows to separately evaluate the impact of an intervention or change in the environment on the longitudinal course of each symptom pattern. Future health effect studies are needed to compare different methods to approach the multidimensional nature of symptom reports, as well as to improve insight in determinants of specific symptom patterns.

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Modeled and perceived exposure to RF-EMF from mobile phone base stations and the development of symptoms over time in a general population cohort.

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Abstract

We assessed associations between modeled and perceived exposure to RF-EMF from mobile phone base stations and the development of non-specific symptoms and sleep disturbances over time. The Dutch population-based Occupational and Environmental Health Cohort study (AMIGO) (n=14829, 31-65 years old) was established in 2011/2012 (T0), with follow up of a subgroup (n=3992 invited) in 2013 (T1, n=2228) and 2014 (T2, n=1740). We modeled far-field RF-EMF exposure from mobile phone base stations at the home address of the participants using a 3D geospatial model (NISMap). Perceived exposure (0=not at all to 6=very much), non-specific symptoms, and sleep disturbance were assessed by questionnaire. We performed cross-sectional and longitudinal analyses, including fixed effects regression. We found small correlations between modeled and perceived exposure in AMIGO at baseline (n=14,309, $r_{Spearman} = 0.10$). For 222 follow-up participants modeled exposure increased substantially (>0.030 mW/m^2) between T0 and T1. This increase in modeled exposure was associated with an increase in perceived exposure in the same time period. In contrast to modeled RF-EMF exposure from mobile phone base stations, perceived exposure was associated with reporting higher symptom scores in both cross-sectional and longitudinal analyses, and with sleep disturbance in cross-sectional analyses.

1. Background

Exposure to radio frequency electromagnetic fields (RF-EMF) from mobile phone base stations has increased rapidly in previous decades. Biological mechanisms responsible for health effects at every day exposure levels are unknown. Systematic reviews (1–4) found no consistent associations between modeled RF-EMF exposure and any individual symptoms or groups of symptoms. A part of the general population (1.5-10%) (5, 6) attributes symptoms such as sleep disturbances, headaches or dizziness to electromagnetic field (EMF) exposure. It is suspected that there may also be psychosocial mechanisms involved (7–10). People have little control over being exposed to RF-EMF from mobile phone base stations, and in combination with uncertainty about potential health risks, this can lead to concern (11, 12) and increased symptom reporting.

Different type of studies have been applied to study effects of RF-EMF exposure from mobile phone base stations on symptoms: laboratory studies (13, 14), and observational studies (15, 16). An important limitation of laboratory studies is that only acute effects of short term exposure can be studied. A limitation of observational epidemiological studies is that the exposure assessment is often inaccurate. Simple proxies have been used for exposure assessment, such as the distance between fixed site transmitters and the home address (17, 18), but these are not sufficiently accurate (19, 20). Using a three dimensional geospatial model is currently the preferred method for assessing personal exposure to far-field RF-EMF exposure from base stations in large populations (19, 21), but application of these models in epidemiological studies has so far been limited. In addition, most observational studies have been cross-sectional, limiting causal inference. Longitudinal studies with accurate exposure assessment are needed to resolve uncertainty about the potential association between far-field RF-EMF exposure and health outcomes (22).

In a cross-sectional study (16) among the general population in the Netherlands over 20% of the participants reported high or extremely high worry about potential health effects from RF-EMF exposure to mobile phone base stations. This study also found that perceived exposure was associated with a higher number of non-specific symptoms when accounting for modeled RF-EMF and extremely low frequency magnetic field exposure. Numerous other studies found associations between symptom reporting and different perceptions (e.g. perceived exposure, perceived risk, worry, concerns, annoyance, or modern health worries), with regard to EMF (4, 9, 16, 23–26), but also with regard to other potential environmental risks (27–32), such as perceived infrasound exposure from wind turbines and perceived air quality. However, most of these studies were cross-sectional and many did not consider actual exposure. One explanation for the association between EMF perceptions and symptom reporting could be a nocebo mechanism, which postulates: The expectation that negative health effects may occur upon exposure can lead to more symptoms. Evidence for this mechanism was seen in provocation studies with sham exposure (9, 26). Conversely, the experience of symptom distress may lead to the search of a cause for these symptoms (33, 34), and increased attention to potential exposures. Attention focusing can amplify the perception of physical signals, a process described as somatosensory amplification (26, 35, 36). Biochemical and psychosocial mechanisms may mutually influence each other (37), and therefore there is added value in considering both modeled and perceived exposure in relation to health outcomes simultaneously and longitudinally.

This is what we set out to do in this prospective cohort study with respect to modeled and perceived exposure to RF-EMF from mobile phone base stations and self-reported non-specific symptoms and sleep disturbance. Figure 1 shows a diagram of the possible relations between the variables of interest. The main research questions that are addressed in this paper are: 1) Is there an association between modeled and perceived exposure to RF-EMF from mobile phone base stations? and 2) How are modeled and perceived exposure associated with non-specific symptoms and sleep disturbances over time? We improve upon previous studies by our longitudinal design, and the combination of modeled exposure and self-reported perceived exposure, in a large sample nested within a community-based cohort that was not recruited specifically for EMF-related questions.

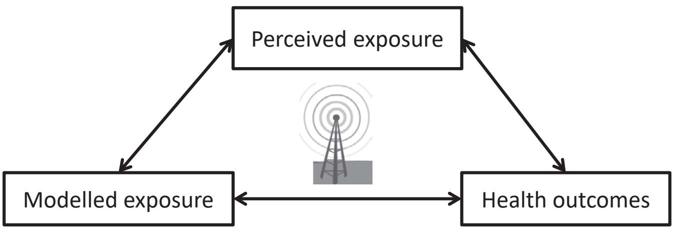

Figure 1. Possible associations between modeled and perceived exposures to far-field RF-EMF from mobile phone base stations and health outcomes (non-specific symptoms and sleep disturbances).

2. METHODS

2.1. Population

This study is nested in the AMIGO cohort, which was set up to study environmental and occupational determinants of diseases and symptoms in the Dutch population (aged 31-65) (see (38) for a full description). From the full cohort, i.e. all participants who were eligible and participated in the questionnaire at baseline (T0 = 2011/2012, n=14829), we invited a subgroup (n=3992) to participate in two follow-up questionnaires (in 2013 (T1) and 2014 (T2)). We based the selection criteria for this subgroup on modeled and perceived exposure to RF-EMF from mobile-phone base stations at baseline in order to achieve exposure contrast: a random selection of 1,429 persons with modeled exposure less than 0.0265 mW/m² and perceived exposure (on a scale of 0–6) less than 2; all subjects with modeled exposure less than 0.0265 mW/m² and perceived exposure greater than 1 (n = 1,272); all subjects with modeled exposure greater than or equal to 0.0265 mW/m² and perceived exposure less than 2(n = 1,069); and all subjects with modeled exposure greater than or equal to 0.0265 mW/m² and perceived exposure greater than 1 (n = 222). Only subjects who participated at T1 (n=2228, response rate 56%) were invited for the T2 questionnaire (n=1740, response rate 78%).

2.2. Modeled exposure

RF-EMF exposure to mobile phone base stations at the geocoded home address was modeled with the 3-dimensional geospatial model NISMap. The applicability of this model for epidemiological studies has been described in a number of previous studies (21, 39–43). The model uses detailed information about 3-dimensional building data, topography, home coordinates, bedroom elevation (exposure modeled 1.5 m above floor height), antenna location, antenna characteristics, and radiation patterns to compute the field strength of GSM900 (Global System for Mobile Communications; European Telecommunications Standards Institute, Sophia-Antipolis, France), GSM1800, and UMTS (Universal Mobile Telecommunications System; 3rd Generation Partnership Project) mobile-phone frequencies. Antenna locations and characteristics were not available for the year 2014, and therefore the exposure estimate only changed in comparison with 2013 in the case of a different home address or bedroom elevation. Therefore, analyses with modeled exposure as predictor of interest are only carried out for T0, T1, and the time interval T0-T1. We calculated the total modeled downlink exposure in mW/m² by summing GSM 900, GSM 1800, and UMTS modeled values (i.e. at time of the study LTE (Long-Term Evolution) was not available in The Netherlands). We did not model exposure at work, because subjects in general spend less than 30% of their time at work, and because exact locations at work are uncertain, in particular for professions that are not bound to one location (e.g. drivers or builders).

2.3. Perceived exposure

Perceived exposure is measured at all time points (T0,T1,T2) with the question: "To what extent are you exposed to (electromagnetic fields/radiation from) base stations for mobile phones, radio or television (scale of 0-6 where 0= not at all, 6= very much)?" Although we did not model exposure to base stations for radio and television, we expected that participants may not be able to distinguish between different type of RF-emitting stations, and therefore included all types of emitters in the perceived exposure question.

2.4. Health outcomes

We assessed two self-reported health outcomes at T0, T1, and T2: non-specific symptoms and sleep disturbances. Similar to another study on EMF and symptoms (44) we used the total symptom score of somatization scale of the 4 dimensional symptom scale (4DSQ-S)(45), which consists of 16 non-specific somatic symptoms (e.g. headaches, low back pain, and dizziness) commonly reported in general practices. According to the 4DSQ manual (45), participants indicated for each symptom whether they were bothered by it during the previous week on a 5-point scale (ranging from no, through to constantly). The scores per symptom were trichotomized and then summed over the symptoms to obtain a total score (no = 0; sometimes = 1, regularly/often/constantly = 2). Sleep disturbances were measured using the sleep scale of the Medical Outcomes Study (MOS). Based on the responses to six sleep items a scale score (sleep index 1: 0-100) was calculated following the instructions described in (46). Higher scores indicate more sleep disturbances, or lower sleep quality.

2.5. Covariates

General information about age, sex, and education was gathered by questionnaire at baseline. We gathered information about neighborhood income (percentage of income earners with a low income in the neighborhood) as an indication of neighborhood socioeconomic status, and degree of urbanization from the Dutch Central Bureau of Statistics (CBS) in 2012 (Key figures neighborhoods).

2.6. Statistical analysis

To answer the first research question we computed the Spearman correlation between modeled and perceived exposure in the full AMIGO cohort. Secondly, we applied linear regression in the subgroup to examine whether participants with an increase in modeled exposure of at least 0.030 mW/m^2 between T0 and T1 (the cutoff point based on the 90th percentile of the distribution of absolute change in modeled RF-EMF exposure to mobile phone base stations) experienced a different change in perceived exposure than the reference group (no change in modeled exposure)

The data from all questionnaires (T0, T1 and T2) were then combined and analyzed with mixed effect regression models (unstructured covariance structure), clustered at the subject level, with a fixed effect for year to adjust for temporal population trends in health outcomes. Four type of models were used in the subgroup to assess cross-sectional and longitudinal associations between perceived and/or modeled exposure with health outcomes; 1) cross-sectional analyses, 2) cohort analyses; 3) change analyses, and 4) fixed effect analyses. The cross-sectional analyses were also done in the full cohort at baseline. In the cohort analyses, we assessed the association between exposure and change in symptoms in the subsequent year. In the change analyses, we examined whether change in exposure over a 1 year period was associated with change in health outcome over the same time period. Perceived exposure and health outcomes were analyzed as continuous variables. Change scores were calculated by subtracting the score between two consecutive years, i.e. T1-T0 and T2-T1). Because of the skewed distribution of modeled exposure, it was analyzed dichotomously in the cross-sectional, cohort and fixed effect analyses. The cutoff point was based on the distribution of modeled total downlink exposure at baseline in the full cohort (low: 0^{th}-90^{th} percentile, high: 90^{th}-100^{th} percentile, cutoff point: 0.050 mW/m²). For the change analyses, we created a variable with 3 categories of modeled exposure based on the distribution of the absolute change in modeled exposure between T0 and T1. We compared the study participants with the 10% largest decrease (upper cutoff point: $-4.571*10^{-4}$ mW/m²) and 10% largest increase (lower cutoff point: 0.030 mW/m²) with the remaining 80% (reference group) for the time interval T1-T0. All models were adjusted for age, sex, urbanization and neighborhood income at baseline and both with or without additional adjustment for exposure (i.e. perceived adjusted for modeled exposure and vice versa). Finally we applied fixed effects regression models (47)(outcome variables respectively DSQ-s score and sleep index), with the predictors perceived exposure (continuous) and modeled exposure (dichotomous). An advantage of this model is that it controls for all stable characteristics of an individual, whether measured or not. However, there is a potential disadvantage for the estimation of the effect of a change in modeled exposure, as an increase in modeled exposure is assumed to have the exact opposite effect of a decrease in modeled exposure, which is not necessarily true.

Missing values (full cohort: ≤4%, subgroup:<1%) were replaced with the most common category (categorical variables), or with the mean (continuous variables). Analyses were carried out using SAS (SAS Institute, Inc., Cary, North Carolina).

3. RESULTS

Table 1 lists the baseline characteristics of the full cohort (n=14,829) and the subgroup (n=3,992) at baseline. Demographics were similar in the full cohort and the subgroup. The exposure and health characteristics at baseline and follow up are shown in Table 2.

Table 1. Baseline Characteristics (T0) of the AMIGO Cohort, Including a Subgroup Also Invited to Complete 2 Additional Follow-Up Questionnaires (T1 and T2), in a Study of Modeled and Perceived Radio-Frequency Electromagnetic Field Exposure From Mobile-Phone Base Stations in Relation to Nonspecific Symptoms and Sleep Disturbances, the Netherlands, 2011/2012

	Full cohort T0 (n=14829)		Subgroup T0 (n=3992)	
	n	Percentage	n	Percentage
Sex				
Male	6561	44.2	1755	44.0
Female	8268	55.8	2237	56.0
Age in years[a]		50.6 (9.4)		50.2 (9.5)
Education				
Low	4546	30.7	1123	28.1
Middle	4627	31.2	1239	31.0
High	5656	38.1	1630	40.8
Neighborhood socioeconomic status[b]		39.4 (6.9)		39.5 (7.4)
Urbanisation				
Very high	1263	8.5	516	12.9
High	3307	22.3	1236	31.0
Moderate	3228	21.8	972	24.3
Low	3615	24.4	867	21.7
Very low	3416	23.0	401	10.0

Abbreviations: AMIGO, Occupational and Environmental Health Cohort Study; SD, standard deviation; SES, socioeconomic status. a Low = primary school/vocational education/community college; intermediate = vocational education/high school;
high = college/university or higher. b Very high = average of >2,500 addresses/km^2; high = average of 1,500–2,500 addresses/km^2; moderate =average of 1,000–<1,500 addresses/km2; low = average of 500–<1,000 addresses/km^2; very low = average of <500 addresses/km^2.

Perceived and modeled exposure were higher in the subgroup than in the full cohort as a consequence of the selection method we applied to increase exposure contrast. There were no significant differences for mean modeled (t-test: t=0.16, p=0.88) or perceived exposure (t-test: t=1.80, p=0.07) at baseline between subgroup participants who completed all follow-up questionnaires and participants who did not complete both follow-up questionnaires. The distribution of change scores from perceived exposure, DSQ-s, and sleep-index are shown in Web Figure 1.

Table 2. Modeled and Perceived Exposure to Radio-Frequency Electromagnetic Fields From Mobile-Phone Base Stations and Symptom Characteristics in the Full AMIGO Cohort (T0) and a Selected Subgroup Invited to Complete 2 Follow-Up Questionnaires (T1 and T2), the Netherlands, 2011–2014

	Full cohort	Subgroup		
Variable	T0 (n=14829)	T0 (n=3992)	T1 (n=2228)	T2 (n=1740)[a]
Modeled exposure (mW/m^2)				
Percentile 10	0.000	0.000	0.000	0.000
Percentile 25	0.000	0.001	0.001	0.001
Percentile 50	0.001	0.007	0.009	0.009
Percentile 75	0.013	0.040	0.051	0.050
Percentile 90[b]	0.050[b]	0.121	0.146	0.137
Perceived exposure[c]	1.0 (1.2)	1.8 (1.6)	1.9 (1.6)	1.8 (1.6)
4DSQ-s	5.9 (5.2)	6.4 (5.5)	6.2 (5.2)	6.1 (5.1)
MOS Sleep-index	27.4 (14.8)	28.3 (15.3)	28.2 (14.7)	27.1 (14.3)

Abbreviations: AMIGO, Occupational and Environmental Health Cohort Study; 4DSQ-S, somatization scale of the Four-Dimensional Symptom Questionnaire; MOS, Medical Outcomes Study; RF-EMF, radio-frequency electromagnetic field; SD, standard deviation.

[a] Transmitter locations and characteristics were not available in 2014; therefore, transmitter data from 2013 were used.

[b] Cutoff point for cross-sectional and cohort analyses.

[c] Perceived exposure was measured on a scale of 0–6, where 0 = not at all and 6 = very much.

We found small correlations between modeled and perceived exposure in the full cohort at baseline ($r_{Spearman} = 0.10$). We compared participants with an increase in modeled exposure between T0 and T1 (absolute change > 0.030 mW/m^2, n=222) with the reference group (10th-90th percentile of the absolute change in modeled exposure, n=1,779) and found a positive association with change in perceived exposure in the same time period (increase in $\beta_{modeled}$ (95% confidence interval) = 0.31 (0.11,0.50), p <0.01). For most of these participants with an increase in modeled exposure this change was due to changes in antennas in the vicinity of their home address; only 15 (7%) of these participants had moved to a new address.

The cross-sectional analyses conducted in the full cohort at T0 (Table 3) and in the subgroup (Table 4) show that perceived, but not modeled exposure is significantly positively associated with both non-specific symptoms and sleep disturbances. In the cohort analyses, we found no associations between either modeled or perceived

Table 3. Associations of Modeled and Perceived Exposure to Radio-Frequency Electromagnetic Fields From Mobile-Phone Base Stations With Nonspecific Symptoms and Sleep Disturbances (linear regression analyses) in the Full AMIGO Cohort (n=14829) At Baseline, The Netherlands, 2011/2012

	DSQ-s score						MOS sleep index					
Predictor	Adjusted[a] β	95% CI	p-value	Unadjusted[b] β	95% CI	p-value	Adjusted[a] β	95% CI	p-value	Unadjusted[b] β	95% CI	p-value
Perceived exposure (0-6)	0.54	0.47,0.61	<0.0001	0.54	0.47,0.61	<0.0001	1.27	1.08,1.46	<0.0001	1.28	1.09,1.47	<0.0001
Modeled exposure (dichotomous)	0.19	-0.07,0.45	0.1610	0.37	0.10,0.64	0.0075	0.56	-0.21,1.33	0.1539	0.98	0.21,1.75	0.0129

Abbreviations: 4DSQ-S, somatization scale of the Four-Dimensional SymptomQuestionnaire; CI, confidence interval;MOS, Medical Outcomes Study.
[a] Adjusted for modeled exposure and perceived exposure, respectively. In addition, all analyses adjusted for baseline values of sex, age, education, neighborhood socioeconomic status,
and urbanization.
[b] Adjusted only for baseline values of sex, age, education, neighborhood socioeconomic status, and urbanization

Table 4. Associations of Modeled and Perceived Exposure to Radio-Frequency Electromagnetic Fields From Mobile-Phone Base Stations With Nonspecific Symptoms and Sleep Disturbances (Mixed Models) in the AMIGO Subgroup Invited to Complete 2 Follow-Up Questionnaires (T0: n = 3,992; T1: n = 2,228; T2: n = 1,740), the Netherlands, 2011–2014

	DSQ-s score						MOS sleep index					
Predictor	adjusted[a] β	95% CI	p-value	unadjusted[b] β	95% CI	p-value	adjusted[a] β	95% CI	p-value	unadjusted[b] β	95%CI	p-value
Cross-sectional												
Perceived exposure	0.28	0.22,0.35	<.0001	0.28	0.22,0.35	<.0001	0.53	0.34,0.72	<.0001	0.53	0.35,0.72	<.0001
Modeled exposure	0.06	-0.26,0.37	0.7170	0.05	-0.27,0.37	0.7588	-0.49	-1.39,0.41	0.2858	-0.52	-1.42,0.39	0.2625
Cohort analyses												
Perceived exposure	-0.03	-0.09,0.03	0.3508	-0.03	-0.09,0.03	0.3493	-0.02	-0.2,0.16	0.8269	-0.02	-0.2,0.16	0.8268
Modeled exposure	0.10	-0.12,0.31	0.3900	0.10	-0.12,0.31	0.3881	0.02	-0.62,0.66	0.9458	0.02	-0.62,0.66	0.9456
Change analyses[c]												
Change in perceived exposure	0.14	0.06,0.22	0.0007	0.14	0.06,0.23	0.0006	0.08	-0.16,0.32	0.5005	0.08	-0.16,0.32	0.4986
Modeled exposure[d,e] decrease	-0.33	-0.86,0.21	0.2271	-0.33	-0.86,0.21	0.2271	-0.56	-2.18,1.07	0.5016	-0.57	-2.19,1.05	0.4908
increase	0.29	-0.24,0.83	0.2831	0.29	-0.24,0.83	0.2823	-0.18	-1.81,1.45	0.8280	-0.21	-1.84,1.41	0.7983

Abbreviations: 4DSQ-S, somatization scale of the Four-Dimensional Symptom Questionnaire; CI, confidence interval; MOS, Medical Outcomes Study.
a Adjusted parameter estimates were adjusted for modeled exposure and perceived exposure, respectively. In addition, analyses were adjusted for baseline values of sex, age, education, neighborhood socioeconomic status, and urbanization, with a fixed effect for year to adjust for temporal population trends in health outcomes. b Unadjusted parameter estimates were adjusted only for baseline values of sex, age, education, neighborhood socioeconomic status, and urbanization, with a fixed effect for year to adjust for temporal population trends in health outcomes. c The parameter estimates in the change analyses represent the change in 4DSQ-S score and MOS sleep index, respectively. d Estimates and P values for the decrease and increase in modeled exposure, respectively, versus the reference group (10th–90th percentiles of the absolute change in modeled exposure: −4.571 × 10−4mWm2 to 0.030mWm2). e The transmitted data that were required as input data for NISMap model estimation were unavailable at T2; therefore, regression coefficients for modeled exposure are provided only for T0 and T1 and the time interval T0-T1.

exposure and change in non-specific symptoms or sleep disturbances one year later (table 4). In the longitudinal change analyses in the subgroup (table 4), an increase in perceived exposure but not modeled exposure was associated with an increase in non-specific symptoms but not sleep disturbances over the same time interval. These results were consistent with the results of the fixed effect models for both non-specific symptoms ($\beta_{perceived} = 0.13$ (95% CI: 0.05, 0.21), $P < 0.01$; $\beta_{modeled} = 0.20$ (95% CI: −0.35, 0.75), $P = 0.47$) and sleep disturbances ($\beta_{perceived} = 0.09$ (95% CI: −0.14, 0.32), $P = 0.48$; $\beta_{modeled} = -0.32$ (95%CI: −1.97, 1.33), $P = 0.70$).

4. DISCUSSION

In this prospective cohort study, we investigated the association between modeled and perceived exposure to RF-EMF from mobile phone base stations and self-reported health outcomes, that is, non-specific symptoms and sleep disturbances. The small correlation between modeled and perceived exposure enabled the investigation of these two measures as conceptually separate predictors for health outcomes. Our results gave no indication that modeled RF-EMF exposure from mobile phone base stations was associated with health outcomes. On the contrary, perceived exposure was associated with higher nonspecific symptom scores as well as more reported sleep disturbances.

4.1. Interpretation of findings

The lack of an association between low modeled RF-EMF exposure levels from mobile phone base stations in the home environment and health outcomes in both the cross-sectional or the longitudinal analyses is in line with most recent previous studies (15, 16, 48). However, modeled exposure may be associated with certain symptoms, but not with the total symptom score. We therefore explored this in secondary cross-sectional logistic regression analyses, for each of the symptoms in the 4DSQ-S scale separately in the full cohort (Web Table 1). Two symptoms (dizziness, pressure or tightness in the chest) were slightly more likely to be reported by exposed than non-exposed participants, but not significantly after adjustment for multiple testing.

Visible exposure sources such as antennas may influence to some extent whether participants think they are exposed, resulting in a weak correlation between modeled and perceived exposure in this study. Interestingly, a substantial increase in modeled exposure in a one year period was associated with a corresponding change in perceived exposure, suggesting that some participants were aware of changes in their environment such as the placement of new antennas.

Perceived exposure was associated with worse health outcomes, in cross-sectional (DSQ-s and Sleep index) and longitudinal change and fixed effect analyses (only DSQ-s scores). Perceived exposure may be influenced by visual cues related to actual exposure, although other factors such as affective reactions to the environment could be more important. Previous studies (49, 50) found that most people have little knowledge about RF-EMF exposure, which can explain the small correlation between modeled and perceived exposure. Not only the perception of being exposed, but also the belief that exposure may be harmful, the extent someone feels concerned about exposures or symptoms, and a number of social and personal factors are probably important to determine whether one develops and/or reports symptoms (10, 26, 51, 52). Higher symptom scores are associated with lower health-related quality of life and increased use of health-care services (53, 54). Adequate risk communication can improve the understanding of EMF exposure for the general population (50) and may prevent the development and/or increased reporting of symptoms in part. However, the pathways between perceived exposure and symptoms may be bidirectional, or perhaps experiencing symptoms typically precedes concern about environmental exposures (33, 34). This may partly explain why our longitudinal cohort analyses did not show temporal precedence of perceived exposure before an increase in symptoms. Other explanations for this effect may be a shorter lag period, or ceiling effects. Subjects with higher perceived exposure already had higher symptom scores at baseline, and were therefore less likely to report even higher symptom scores in the following questionnaire.

Despite our finding that modeled RF-EMF exposure from mobile phone base stations was not associated with health outcomes, it remains important to consider the role of both RF-EMF exposure sources in the environment and perceived exposure. Our results suggest that especially a change in the presence of antenna's in the home environment may increase perceived exposure, and possibly also indirectly influence symptom scores in individuals. Complicated relationships between exposure sources, actual exposure, perception, and the development of symptoms also exist for other environmental exposures. For noise exposure, prior studies found that the association between modeled exposure to noise from road traffic and symptom score was mediated by noise annoyance (55, 56). There is a need for more multidisciplinary studies that consider the role of both actual environmental exposures and perception in relation to self-reported health outcomes.

4.2. Strengths

Our study design had several strengths, allowing for robust conclusions regarding potential effects of perceived and modeled exposure to mobile phone base stations on the experience of non-specific symptoms and sleep disturbances. The main strength of our study was the prospective design. Secondly, the study sample was large, and we oversampled high exposed subjects, which produced adequate statistical power for assessment of potential health effects of RF-EMF from mobile phone base stations in the general population. Thirdly, the AMIGO cohort (38) was setup with the broad purpose to study occupational and environmental exposures in relation to health outcomes in the general population. Therefore, the participants were probably not aware of the focus on EMF. Finally, we used the NISMap model, with detailed input data (home coordinates, bedroom elevation, antenna characteristics) to estimate RF-EMF exposure to mobile phones in the bedroom at the home address. NISMap is able to meaningfully rank participants on modeled exposure (21, 40, 41, 43), although there can be substantial misclassification.

4.3. Limitations

This study has limitations. Importantly, RF-EMF exposure at locations other than the home address was unknown. Secondly, in contrast to modeled exposure, the measure of perceived exposure also included perceived exposure to RF-EMF from base stations for radio and TV, because subjects in general have little knowledge about different types of transmitters (50). Furthermore, we modeled RF-EMF exposure at home, yet subjects reported perceived RF-EMF exposure from base stations in general, which could include base stations they usually come across at work, during commuting and leisure time. For these two reasons, we may have slightly underestimated the association between modeled and perceived exposure. However, the chance that subjects indeed referred to radio and TV base stations is relatively low, given that they are much less abundant than mobile phone base stations. We did not consider RF-EMF exposure from other sources than mobile phone base stations. Therefore, we cannot exclude the possibility that total RF-EMF exposure is associated with symptoms. However, including other exposure sources was not feasible for this particular study because of the aim to compare effects of modeled and perceived exposure. Correlations between modeled and perceived exposure may be different for other sources. Additionally, the associations of perceived or modeled exposure with health outcomes could be different for other RF-EMF sources.

4.4. Conclusion

The results of our nationwide prospective study showed that not modeled exposure but perceived exposure to mobile phone base stations is a predictor of nonspecific symptoms and sleep disturbances. Awareness of the presence of mobile phone base stations in the home environment may play an indirect role in symptom reporting, through effects on perceived exposure. Our robust study design adds to the body of evidence that there seems to be no substantial adverse effect of every day residential

RF-EMF exposure levels from mobile phone base stations on the development of non-specific symptoms and sleep disturbance in the general public.

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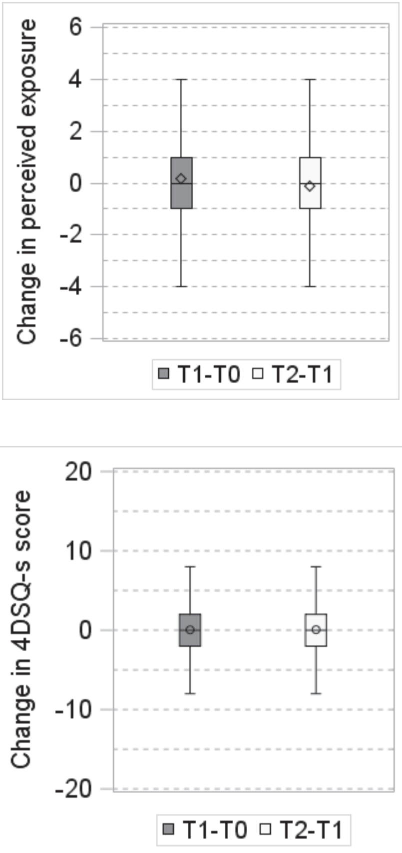
Supplemental material



Web Figure 1. Distribution of changes in 1) perceived exposure, 2) Four-Dimensional Symptom Questionnaire (DSQ-s), and 3) sleep index for each time interval. Rhombs mark mean values, horizontal lines mark median values, inner boxes show the 25%–75% quantiles, and the outer lines show the 1.5 interquartile range of the lower/upper end of the inner box.

Web Table 1. Logistic Regression in the Full AMIGO Cohort (*n* = 14,829) at Baseline: Effects of Modeled and Perceived Exposure to Mobile-Phone Base Stations on *Individual Symptoms*

	Odds Ratio (95% Confidence Interval)	
Health Outcome	**Modeled Exposure (Dichotomous, Cutoff 90th Percentile)**	**Perceived Exposure (0–6)**
Dizziness	1.14 (1.02, 1.29)	1.15 (1.12, 1.18)
Pain in muscles	0.97 (0.87, 1.09)	1.11 (1.07, 1.14)
Fainting	0.84 (0.55, 1.31)	1.22 (1.12, 1.34)
Neck pain	1.03 (0.92, 1.15)	1.14 (1.11, 1.17)
Back pain	1.06 (0.95, 1.19)	1.08 (1.05, 1.11)
Excessive sweating	1.09 (0.97, 1.22)	1.09 (1.05, 1.12)
Palpitations	1.07 (0.94, 1.22)	1.17 (1.14, 1.21)
Headache	1.04 (0.93, 1.16)	1.09 (1.06, 1.12)
Bloated feeling in abdomen	0.99 (0.89, 1.11)	1.13 (1.09, 1.16)
Blurred vision	1.00 (0.89, 1.14)	1.14 (1.11, 1.18)
Shortness of breath	1.10 (0.95, 1.27)	1.14 (1.10, 1.19)
Nausea	1.03 (0.90, 1.17)	1.16 (1.12, 1.20)
Pain abdomen	1.08 (0.95, 1.23)	1.14 (1.10, 1.18)
Tingling fingers	0.99 (0.87, 1.13)	1.16 (1.12, 1.19)
Tight feeling in chest	1.22 (1.05, 1.42)	1.16 (1.12, 1.20)
Chest pain	1.07 (0.89, 1.28)	1.15 (1.10, 1.20)

AMIGO, Occupational and Environmental Health Cohort Study.
Analyses were adjusted for perceived, respectively modeled exposure. In addition, all analyses in this table were adjusted for sex, age, education, neighborhood socioeconomic status, and urbanization.

Longitudinal associations between risk appraisal of base stations and non-specific symptoms

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Submitted

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Abstract

Introduction: Studies found that higher risk appraisal of radiofrequency electromagnetic fields is associated with reporting more non-specific symptoms such as headache and back pain. There is limited data available on the longitudinal nature of such associations and what aspects of risk appraisal and characteristics of subjects are relevant.

Objective: To examine cross-sectional and longitudinal associations between risk appraisal measures and non-specific symptoms, and assess the role of subject characteristics (sex, age, education, trait negative affect) in a general population cohort.

Methods: This study was nested in the Dutch general population AMIGO cohort that was established in 2011/2012, when participants were 31-65 years old. We studied a sample of participants (n=1720) who filled in two follow-up questionnaires in 2013 and 2014, including questions about perceived exposure, perceived risk, and health concerns as indicators of risk appraisal of base stations, and non-specific symptoms.

Results:
Perceived exposure, perceived risk, and health concerns, respectively, were associated with higher symptom scores in cross-sectional and longitudinal analyses. Only health concerns (not perceived exposure and perceived risk) temporally preceded high symptom scores and vice versa. Female sex, younger age, higher education, and lower trait negative affect were associated with higher risk appraisal of mobile phone base stations.

Discussion:
The findings in this study strengthen the evidence base for cross-sectional and longitudinal associations between higher risk appraisal and non-specific symptoms in the general population. However, the directionality of potential causal relations in non-sensitive general population samples should be examined further in future studies, providing information to the benefit of risk communication strategies.

1. Introduction

On average people report more non-specific symptoms such as headache or dizziness when they think they are exposed to radiofrequency electromagnetic fields (RF-EMF) from base stations, regardless of actual level of exposure (1–5). Several studies examined the underlying psychosocial mechanisms in experimental studies with sham exposure (2, 5–8). However, there is a need for more prospective population studies to gain insight in the direction(s) of associations in a general population context.

People form mental models of base stations in their living environment (9). These internal representations of the external reality shape reasoning, decision making, and behavior and can play a role in individual health responses to the environment (10, 11). Mental models of base stations can include beliefs about exposure and potential health risks, which often do not correspond with the view of experts (12, 13). For example, there are low correlations between perceived RF-EMF exposure levels on one hand and measured or modelled exposure levels on the other hand (3, 4, 14–16). At the same time, many people are concerned about potential health risks from EMF (3, 17–19). They associate EMF exposure with perceived health risks such as cancer, but also with non-specific symptoms such as dizziness or concentration problems, and with sleep disturbance (1, 18, 20–22). These concerns do not match the results of epidemiological research, which does not indicate clear adverse health effects of RF-EMF exposure from base stations at every day levels of exposure (4, 23–25). If health effects exist at every day exposure levels, these are likely to be small, and to occur in small (sensitive) groups that have not been identified yet. We will use the term risk appraisal as an overarching term for individual perceptions about personal exposure, health risks, and concerns for personal health. These perceptions can play a role in individual health responses to a potential health hazard (26, 27), regardless of any disparities with epidemiological findings.

A number of studies, mostly experimental studies and studies with electro hypersensitive participants, have examined the link between risk appraisal and increased symptom reporting. There is evidence for the existence of nocebo effects, especially in situations with sham exposure (2, 16), or when there is a visible change in the environment such as the placement of a new base station or power line (27, 28). A nocebo response is the counterpart of placebo, i.e. an adverse health response after a treatment or exposure that is not a direct result of this exposure (29). Based on studies with people who report electro hypersensitivity (6, 30) or idiopathic environmental intolerance (31) there is evidence of a circular process where somatosensory amplification plays a role in amplifying symptoms and risk perception. Other processes may also be important, for instance people who experience many symptoms may be more likely to attribute their symptoms to exposures to an environmental exposure, and become more aware of, and concerned about environmental exposures including EMF (Dieudonné, 2016). This increased awareness has been described as environmental monitoring (Köteles and Simor, 2013). Although experimental studies are important for understanding which psychosocial mechanisms could explain the link between risk appraisal and increased symptom reporting, there is a need for more prospective studies in the general population. With prospective studies, it may be possible to gain insight in the direction(s) of associations and the relative importance of mechanisms such as nocebo and incorrect attribution in the general population. This insight is important for the development of adequate risk communication strategies, as well as for the interpretation of possible indirect health effects of exposure, or exposure sources, through risk appraisal. For example, the placement of a new base station could have a negative impact on symptom experiences through increases in perceived exposure (4), but this phenomenon is difficult to disentangle from incorrect attribution of existing or new symptoms to this new exposure source.

Subject characteristics such as sex, age, education, and trait negative affect have been shown to influence both symptom scores and risk appraisal (26). For example, women consistently report higher risk appraisal and more symptoms than men (34, 35). As a trait, higher negative affect is associated with higher levels of risk appraisal as well as with reporting more symptoms (31, 36–39). For other subject characteristics (f.i. education level, race, age) the results regarding risk appraisal are inconsistent across studies, different measures, and type of risks (1, 35, 40–46). For example, education was associated with higher risk appraisal of mobile phone base stations (46) and smoking (47) but negatively with risks in general (41, 44). The inclusion of the role of subject characteristics in this prospective study will achieve a more comprehensive understanding of risk appraisal of base stations and its link with symptom reporting.

The first objective of this study was to examine cross-sectional and longitudinal associations between risk appraisal of RF-EMF exposure from base stations and the experience of non-specific symptoms in a prospective general population cohort. We considered different aspects of risk appraisal with respect to RF-EMF from mobile phone base stations, namely perceived personal exposure in the residential environment, perceived risk that exposure could be a health risk in general, and concerns regarding personal health risks. Secondly, we examined the influence of a number of subject characteristics (sex, age, education, and trait negative affect) on risk appraisal and symptom score.

2. Method

2.1 Population

This study is nested in the AMIGO cohort, which was setup in 2011/2012 (n=14,829) to study environmental and occupational determinants of diseases and symptom reporting in the general population (see (48) for a full description). The participants were not specifically recruited for EMF related topics. We studied a follow-up sample of the cohort that participated in two additional questionnaires (in 2013 (defined here as T1) and 2014 (defined here as T2). The selection strategy for the invitations to participate in the follow-up sample is described in detail elsewhere (4). In short, the purpose of this selection was to achieve contrast in both modelled (as a proxy of exposure) and perceived exposure to RF-EMF from mobile phone base stations. This was achieved by oversampling subjects with high modelled, and/or high perceived exposure at T0. Only participants who answered all questions regarding symptoms, concerns, risk perception, perceived exposure, and negative affect at both T1 and T2 were included in this study (n=1720). This resulted in the exclusion of n=484 participants who participated at T1 but not at T2, and the exclusion of an additional n=24 participants with missing responses on one or multiple key variables.

2.2 Non-specific symptoms

At T1 and T2 we assessed the total symptom score with the somatization scale of the 4 dimensional symptom scale (4DSQ-S), which consists of 16 non-specific somatic symptoms commonly reported in general practices (e.g. headaches, low back pain, and dizziness). According to the 4DSQ manual (49), participants indicated for each symptom whether they were bothered by it during the previous week on a 5-point scale (ranging from no, through to constantly). The scores per symptom were trichotomized and then summed over the symptoms to obtain a total score (no = 0; sometimes = 1, regularly/often/constantly = 2).

2.3 Risk appraisal of RF-EMF exposure to base stations

We assessed risk appraisal of RF EMF from base stations at T1 and T2 with three separate items: 1) Perceived exposure: "To what extent do you think are you exposed to (electromagnetic fields/radiation from) base stations for mobile phones, radio or television (scale of 0-6 where 0= not at all, 6= very much)?". 2) Perceived risk: "To what extent do you think that (electromagnetic fields/radiation from) base stations for mobile phones, radio or television can be a health risk in everyday situations (scale of 0-6 where 0= not at all, 6= very much)?". 3) Concerns: "To what extent are you concerned about your own health because of (electromagnetic fields/radiation from) base stations for mobile phones, radio or television (scale of 0-6 where 0= not at all, 6= very much)?".

2.4 Subject characteristics

The baseline questionnaire in 2011/2012 included questions on sex, date of birth (to calculate age), and education level. We assessed trait negative affect at T2 with a Dutch version of the I-PANAS-SF (50). This scale consists of ten items (five positive and five negative) such as alert, upset, ashamed. Participants were asked how often (never – always) they experience each of these feelings. A total score for negative affect was calculated from the five negative items. A higher score indicates more negative affect. Positive affect was not analyzed as it fell beyond the scope of this study.

2.5 Statistical Analyses

The data were analyzed using SAS enterprise guide 6.1 software. We first performed cross-sectional analyses. Multifactor Analysis Of Variance (ANOVA) was used to measure mean differences for sex, age, education and negative affect in risk appraisal (perceived exposure, perceived risk, and concerns) and symptom scores. Next, we examined the correlations among variables of interest by calculating Spearman correlations. The data from both questionnaires were then combined and analyzed with multivariate mixed effect regression models clustered at the subject level with a fixed effect for year to adjust for temporal population trends in total DSQ-s symptom score. Risk appraisal indicators and individual characteristics (sex, age, education, negative affect) were included as predictors. Risk appraisal indicators were included jointly in the multivariate models presented in Table 3, and in separate models in the tables presented in Table 4. We then studied the longitudinal associations between risk appraisal and symptom score with two different types of models. With the first type, the autoregressive linear models, we examined a time lag of one year between risk appraisal indicators and symptom score, and vice versa. These models examined whether the risk appraisal indicators perceived exposure, risk perception and concerns, respectively, at T1 were associated with symptom score at T2 (adjusting for symptom score at T1), and whether symptom score at T1 were associated with perceived exposure, risk perception and concerns, respectively, at T2 (adjusting for T1 values). The second type of longitudinal analyses were fixed effect analyses, where we examined the intra-individual variation in risk appraisal (T2-T1) on the one hand and symptom score (T2-T1) on the other. Fixed effect models only consider within individual variation, effectively adjusting for unmeasured time invariant confounders (51–53).

3. Results

3.1 Subject characteristics

The population characteristics are reported in table 1. Age and negative affect are presented categorically for presentation in this table. Slightly more women (53%) than men participated in this study. The most common age category was 51-60 years (37%, at T1). A large portion of the sample had a high education (46%). The results of the

Table 1. Participant Characteristics, risk appraisal and symptom scores in AMIGO follow-up sample at T1 (2013), n=1720

		Perceived exposure T1 mean (SD)	Perceived risk T1 mean (SD)	Perceived concerns T1 mean (SD)	Symptom score T1 mean (SD)
Gender					
Male	n=804 (47%)	1.69 (1.54)	1.77 (1.63)	1.33 (1.51)	5.41 (5.03)
Female	n=916 (53%)	2.05 (1.58)	2.35 (1.74)	1.70 (1.69)	6.56 (4.83)
p-value*		<0.0001	<0.0001	<0.0001	<0.0001
Age (in years)					
31-40	n=192 (11%)	2.39 (1.44)	2.48 (1.61)	1.64 (1.57)	5.75 (4.46)
41-50	n=437 (25%)	2.03 (1.54)	2.31 (1.72)	1.57 (1.61)	5.73 (4.80)
51-60	n=630 (37%)	1.86 (1.56)	2.10 (1.72)	1.56 (1.63)	6.52 (5.26)
>60	n=461 (27%)	1.55 (1.59)	1.65 (1.65)	1.39 (1.61)	5.72 (4.84)
p-value*		<0.0001	<0.0001	0.166	0.008
Education					
Low	n=439 (25%)	1.69 (1.55)	1.84 (1.63)	1.55 (1.66)	7.41 (5.72)
Middle	n=487 (28%)	1.87 (1.59)	2.14 (1.74)	1.62 (1.63)	6.09 (4.87)
High	n=794 (46%)	1.99 (1.56)	2.17 (1.74)	1.45 (1.58)	5.21 (4.35)
p-value*		0.003	0.002	0.177	<0.0001
Negative affect [a]					
Lowest tertile	n=558 (33%)	1.71 (1.58)	1.91 (1.75)	1.29 (1.56)	4.51 (4.18)
Medium tertile	n=521 (30%)	1.78 (1.52)	1.98 (1.70)	1.38 (1.53)	5.40 (4.20)
Highest tertile	n=641 (37%)	2.11 (1.57)	2.29 (1.67)	1.85 (1.68)	7.84 (5.56)
p-value*		<0.0001	0.0001	<0.0001	<0.0001

*P-values show the significance of effects in multifactor ANOVAs. First and higher order interactions between factors were not significant.

[a] Negative affect is presented categorically in this table and was assessed at T2 (2014)

multifactorial ANOVAs (Table 1) show the influence of subject characteristics on risk appraisal and symptom scores at T1. Overall, men had lower indicators of risk appraisal than women and reported lower symptom score ($p<0.0001$). Risk appraisal scores were lower for older participants. Participants with a low education reported lower indicators of risk appraisal and higher symptom scores than participants with a high education. Differences in risk appraisal by age and education were significant for perceived exposure and perceived risk but not for concerns. Negative affect was associated with higher risk appraisal and higher symptom scores. First and higher order interaction effects (results not presented) between subject characteristics were not significant.

3.2 Risk appraisal and symptom score

The means of and correlations among variables of interest are presented in Table 1 (with ANOVA of means by subject characteristics) and Table 2 (overall means and Spearman correlations). Note that reported mean scores were not representative of the means in the full AMIGO cohort due to the sampling strategy based on perceived (and modelled) exposure. The Spearman correlations over time among variables measured at T1 and T2 ranged from 0.55 (risk perception) to 0.77 (DSQ-s symptom scores). Correlations between different aspects of risk appraisal at the same point in time ranged from 0.58 to 0.68.

Table 2. Spearman Correlations and overall means and standard deviations in AMIGO follow-up sample that completed questionnaires at T1 (2013) and T2 (2014), (N=1720)

	perceived exposure T1	perceived exposure T2	risk perception T1	risk perception T2	concerns T1	concerns T2	Symptoms T1	Symptoms T2	negative affect	mean (sd)
perceived exposure T1	-									1.88 (1.57)
perceived exposure T2	0.63	-								1.76 (1.64)
risk perception T1	0.63	0.49	-							2.08 (1.71)
risk perception T2	0.44	0.60	0.55	-						2.06 (1.74)
concerns T1	0.58	0.51	0.67	0.50	-					1.53 (1.62)
concerns T2	0.45	0.59	0.48	0.68	0.60	-				1.51 (1.61)
Symptoms T1	0.13	0.11	0.11	0.07	0.15	0.14	-			6.02 (4.96)
Symptoms T2	0.10	0.12	0.09	0.11	0.14	0.17	0.77	-		6.10 (5.06)
negative affect T2	0.12	0.19	0.12	0.18	0.18	0.24	0.35	0.41	-	8.99 (2.82)

Darker blue colors represent stronger correlations, lighter blue colors represent weaker correlations.

Table 3. Results of Multivariate Mixed models with Symptom score as dependent variable in AMI-GO follow-up sample that completed questionnaires at T1 (2013) and T2 (2014), (N=1720)

Predictor(s)	model 1. with year, gender, age and education		model 2. with year, gender, age, education, Negative Affect	
	Parameter estimate (CI)	p-value	Parameter estimate (CI)	p-value
Perceived exposure[a]	0.17 (0.06, 0.27)	0.002	0.13 (0.03, 0.24)	0.013
Perceived risk[a]	0.09 (-0.01, 0.19)	0.079	0.09 (-0.01, 0.19)	0.089
Concerns[a]	0.13 (0.02, 0.24)	0.081	0.05 (-0.05, 0.16)	0.305
year of questionnaire (T2)	0.11 (-0.05, 0.27)	0.183	0.10 (-0.06, 0.26)	0.207
female gender	0.91 (0.47, 1.35)	<.0001	0.58 (0.17, 0.98)	0.006
age	0.00 (-0.03, 0.02)	0.925	0.02 (-0.01, 0.04)	0.146
Medium education[b]	-1.25 (-1.85, -0.66)	<.0001	-1.07 (-1.62, -0.52)	0.0001
High education[b]	-2.20 (-2.75, -1.66)	<.0001	-1.99 (-2.50, -1.49)	<.0001
Negative affect			0.64 (0.57, 0.71)	<.0001

Predictors are mean centered
[a] Likert Scale 0 = not at all to 6 = very much
[b] The reference category is low education

Multivariate models including the three risk appraisal items (Table 3) showed that perceived exposure and concerns explained unique variance in symptom scores, despite the correlations between these predictors. The regression coefficient for the effect of risk appraisal on symptom score was smaller when negative affect was included in the model (Table 3), in particular for concerns. Perceived risk was redundant in the multivariate model, as well as concerns when negative affect was included (Table 3). All risk appraisal variables were significant when included in separate models (Table 4). Interaction effects between risk appraisal and individual characteristics were examined in additional analyses (results not presented), but did not result in improved model fit.

In the longitudinal autoregressive analyses (Table 5) we found that concerns at T1 were significantly associated with higher symptom score at T2 (adjusted for symptom score at T1), and that symptom score at T1 was associated with more concerns at T2 (adjusted for concerns at T1). In contrast, we found no association between perceived exposure or perceived risk at T1 and symptom score at T2, adjusting for symptom score at T1. Also, the associations between symptom score at T1 and perceived exposure or perceived risk at T2 were not significant (adjusting for baseline values of perceived exposure, respectively perceived risk). The results of fixed effect analyses are presented in Table 6. Intra-individual variation in risk appraisal scores over time was associated with intra-individual variation in symptom scores in the same time period.

Table 4. Results of separate Mixed models for each risk appraisal indicator (perceived exposure, perceived risk, and concerns) with symptom score as dependent variable in AMIGO follow-up sample that completed questionnaires at T1 (2013) and T2 (2014), (N=1720)

	Perceived exposure		Perceived risk		Concerns	
Predictor(s)	Parameter estimate (CI)	p-value	Parameter estimate (CI)	p-value	Parameter estimate (CI)	p-value
indicator risk appraisal	0.20 (0.11, 0.29)	<.0001	0.17 (0.09, 0.25)	<.0001	0.16 (0.07, 0.25)	0.0003
year (T2)[a]	0.11 (-0.05, 0.27)	0.183	0.09 (-0.07, 0.24)	0.283	0.09 (-0.07, 0.25)	0.295
female gender	0.61 (0.20, 1.01)	0.003	0.61 (0.20, 1.01)	0.004	0.63 (0.23, 1.04)	0.002
age	0.02 (-0.01, 0.04)	0.161	0.02 (-0.01, 0.04)	0.186	0.01 (-0.01, 0.03)	0.272
Medium education[b]	-1.06 (-1.61, -0.51)	0.0002	-1.06 (-1.61, -0.51)	0.0002	-1.04 (-1.59, -0.49)	0.0002
High education[b]	-2.00 (-2.50, -1.50)	<.0001	-2.00 (-2.50, -1.50)	<.0001	-1.93 (-2.43, -1.43)	<.0001
Negative affect	0.65 (0.57, 0.72)	<.0001	0.65 (0.58, 0.72)	<.0001	0.64 (0.57, 0.72)	<.0001

Predictors are mean centered.
[a] The reference category is T1 (2013)
[b] The reference category is low education.

Table 5. Results of Autoregressive analyses for longitudinal associations between Symptom score and each risk appraisal indicator in AMIGO follow-up sample that completed questionnaires at T1 (2013) and T2 (2014), (N=1720)

Model	Outcome variable	Predictors	Estimate	P-value
1	Symptom score T2	Symptom score T1	0.79 (0.76,0.82)	<0.0001
		Perceived exposure T1	-0.006 (-0.10,0.10)	0.96
2	Symptom score T2	Symptom score T1	0.79 (0.76,0.82)	<0.0001
		Perceived risk T1	0.02 (-0.07,0.10)	0.73
3	Symptom score T2	Symptom score T1	0.78 (0.75,0.81)	<0.0001
		Concerns T1	0.10 (0.00,0.19)	0.04
4	Perceived exposure (0-6)[a] T2	Perceived exposure T1	0.65 (0.62,0.69)	<0.0001
		Symptom score T1	0.01 (-0.01,0.02)	0.25
5	Perceived risk (0-6)[a] T2	Perceived risk T1	0.56 (0.52,0.60)	<0.0001
		Symptom score T1	0.00 (-0.01,0.02)	0.58
6	Concerns(0-6)[a] T2	Concerns T1	0.60 (0.56,0.63)	<0.0001
		Symptom score T1	0.02 (0.00,0.03)	0.01

[a] Likert Scale 0 = not at all to 6 = very much

Table 6. Results of Fixed effect models* for associations between intra-individual variation over time in risk appraisal indicators and symptom score in AMIGO follow-up sample that completed questionnaires at T1 (2013) and T2 (2014), (N=1720).

Models	Predictor(s)	Parameter estimate (CI)	p-value
1	Perceived exposure (0-6)[a]	0.17 (0.05, 0.29)	0.004
2	Perceived risk (0-6)[a]	0.17 (0.08, 0.27)	0.0004
3	concerns (0-6)[a]	0.12 (0.01, 0.23)	0.039

[a] Likert Scale 0 = not at all to 6 = very much
*These fixed effect models only consider within individual variation over time, effectively adjusting for unmeasured time invariant confounders.

4. Discussion

We studied the cross-sectional and longitudinal associations between risk appraisal of base stations and non-specific symptoms and the influence of subject characteristics in a prospective general population cohort. Risk appraisal (perceived exposure, perceived risk, personal health concerns) of RF-EMF from base stations was associated with higher symptom scores in cross-sectional and longitudinal analyses. In addition, we showed that subject characteristics in sex, age, education, and trait negative affect were related to both risk appraisal and symptom scores.

4.1 Interpretation risk appraisal-symptom score association

In our study we showed cross-sectional and longitudinal associations between risk appraisal of base stations and symptom reporting in a general population sample, despite the relatively low mean levels of risk appraisal. Previous studies found similar associations between risk appraisal of EMF and symptom scores (2, 3, 6, 27, 32), but most of these studies were experimental, cross-sectional or in specific sub-populations. With longitudinal analyses we aimed to improve our understanding of the directionality of the associations between risk appraisal and symptom scores. Health concerns, but not perceived exposure nor perceived risk, were associated with reporting more symptoms one year later, adjusting for baseline values of the dependent variable. And, vice versa, symptoms were positively associated with reporting more concerns one year later. In the longitudinal fixed effect models, we showed that intra-individual variation between T1 and T2 in risk appraisal scores was associated with intra-individual variation in symptom scores in the same period. These longitudinal analyses show that there are possibly bidirectional causal associations between risk appraisal and symptom scores. An alternative explanation for this result however, could be an unmeasured variable, that changes over time within individuals, and is correlated with both risk appraisal and symptom reporting (for example: current negative feelings). Interestingly, we found some evidence suggesting that at least for personal health concerns, mechanisms in both directions can occur in a general population sample. This would indicate that previously proposed psychosocial mechanisms such as nocebo, incorrect attribution and environmental monitoring are simultaneously responsible for the associations between risk appraisal and symptom reporting in the general population. It will be interesting to further explore to what extent these mechanisms complement and reinforce each other. Although considered in some studies (32, 33) reversed causation mechanisms such as incorrect attribution have not received much attention in prior studies. The role of such mechanisms could be of importance for the effectiveness of intervention strategies targeted at lowering high risk appraisal scores, and for the interpretation of associations between risk appraisal and symptom scores. In future studies, for example with a larger number of repeated measurements and shorter time intervals, may aid the understanding of how these mechanisms occur together and complement each other.

4.2 Subject characteristics

We showed that women, younger participants, participants with a moderate to higher education and higher trait negative affect reported higher risk appraisal scores. Symptom scores were higher for women, for participants with a low education, and for participants high in negative affect. The effect of education level on risk appraisal deserves further study. Previous studies (41, 44, 54) generally reported lower risk appraisal for demographic groups with more power in society, including individuals with a higher education. Our results showed that this principle does not apply to all type of risks, at least not to risk appraisal of RF-EMF from base stations. Possibly, there is a lower familiarity with mobile phone base stations as a potential health risk among participants with a lower education, which may have resulted in lower risk appraisal scores for this group.

4.3 Different measures of risk appraisal

Previous studies (3, 26, 55, 56) often focused on a single aspect of risk appraisal, for example perceived exposure or worry about a risk. In this study we analyzed three different aspects of risk appraisal regarding RF-EMF: perceived personal exposure, perceived risks in general, and concerns about personal health. These items differed conceptually on two dimensions, respectively personal versus general and cognitive versus affective perception. Perceived exposure and concerns addressed the personal situation of the participant, while perceived risk focused on the potential health risk of RF-EMF in general. Perceived exposure ("To what extent do you think you are exposed to..") and perceived risk ("To what extent do you think that… is a health risk") predominantly reflected cognitive elements of risk appraisal, while concerns for personal health reflected affective elements (57). Although the results consistently showed positive associations between risk appraisal and symptoms, regardless of the particular risk appraisal item, there were subtle differences between the results of different analyses. We found higher overall means for perceived risk than for the other two items, in line with research showing that people perceive others as more vulnerable to potential risks than themselves (58, 59). Correlations with trait negative affect were slightly higher for the more affective item concerns than for perceived exposure and perceived risk. In addition, concerns became redundant when negative affect was taken into account in the multivariate mixed models (Table 3), indicating greater overlap with the effect of trait negative affect than the other two items. On the other hand, only for concerns we found evidence of temporal precedence of reporting concerns before an increase in symptom score and vice versa. Thus, using different items to assess risk appraisal might lead to slightly different conclusions, which advocates the use of multiple items in future studies to thereby refine the interpretation of the underlying processes.

4.4 Strengths

Our study had a number of strengths. First, it is one of the few large longitudinal general population studies concerning risk appraisal and symptom reporting. Secondly, as discussed above, we used different measures to assess risk appraisal, and therefore we were able to compare these measures and study their associations with symptom reporting. Thirdly, the AMIGO cohort was recruited to study occupational and environmental health in general and therefore subjects were not prompted to participate in an EMF and health study which could have resulted in biased responses. Moreover, the questions on risk appraisal were embedded within a list of other environmental exposures, such as traffic-related air pollution and noise. Nevertheless, the responses of participants were not completely representative of a general population sample, due to the follow-up selection strategy of oversampling participants with high perceived and modelled exposure. This sampling strategy likely did not result in the selection of a large number of self-identified electro hypersensitive participants. In the survey questionnaires, participants were asked whether they attributed any health problems to an environmental exposure, and if so, they were subsequently asked which environmental exposure and what kind of health problems. The list of potential attributions included EMF exposure sources and free text ‘other environmental causes’. In the full AMIGO cohort (n=14829), 84 participants attributed health problems to any sort of EMF exposure at baseline (2011/2012 questionnaire). They were all invited for the follow-up questionnaires used in this study, and 27 of them did participate in the follow-up questionnaires. Only six of these participants still reported attribution of health problems to EMF exposure at both follow-up surveys (T1 and T2). Finally, in previous work (4) we did not find associations between modelled (“actual”) RF-EMF exposure from mobile phone base stations and symptom reports in the AMIGO cohort. The exposure model

NISMap that was used to assess RF-EMF exposure from mobile phone base stations was previously validated for use in epidemiological studies (60). Therefore, we could be fairly certain that actual exposure did not confound the association between risk appraisal and symptom score in our current study sample.

4.5 Limitations

This study also had a number of limitations. The questionnaires were spaced apart for approximately a year, and it is not certain what lag period is relevant to study longitudinal associations between risk appraisal and symptom scores. Secondly, trait negative affect (T2) was only measured at a single point in time. However, the associations of negative affect with risk appraisal and symptom scores were stronger when measured in the same questionnaire, indicating that the negative affect measure captured both stable ("trait") and occasion specific ("state") variance. The mixed model analyses included risk appraisal and symptom scores at T1 and T2, but included "trait" negative affect only measured at T2. As a result, we overestimated the effect of "trait" negative affect, because a portion of the "state" variance in negative affect was included in the parameter estimates. Finally, we focused on risk appraisal of RF EMF from mobile phone base stations. Studies using measures such as modern health worries show that perceptions of different risks are highly correlated (36) as they are presumed to be part of a more general overarching mental model. Thus, it remains interesting to further study how specific our results on risk appraisal and symptom reporting are for RF-EMF from base stations, as we did not consider risk appraisal of other risks.

4.6 In summary

In conclusion, this study shows that risk appraisal of mobile phone base stations is cross-sectionally and longitudinally associated with increased symptom reporting in a general population sample. This finding is of interest to public health, as non-specific symptoms are very common in the population, and are associated with a lower quality of life and increased health care use (61, 62). However, the directionality of potential causal relations in non-sensitive general population samples should be examined further in future studies, providing more information to the benefit of risk communication strategies.

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Modeled and perceived RF-EMF, noise and air pollution and symptoms in a population cohort. Is perception key in predicting symptoms?

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Abstract

Psychosocial research has shown that perceived exposure can have an influence on symptom reporting, regardless of actual exposure. The impact of this phenomenon on the interpretation of results from epidemiological research of environmental determinants on self-reported health is unclear and understudied. We examined the interplay between environmental exposures, the perceived level of these exposures, and reported symptoms, for three different exposures in a prospective cohort study. Spearman correlations between modeled and perceived exposure were substantial for air pollution (r_{Sp}=0.34) and noise (r_{Sp}=0.40). These findings were less distinct for radiofrequency electromagnetic fields (RF-EMF) (r_{Sp}=0.11). The exposures varied in the degree to which they can be sensorially observed, and in the plausibility of the link with different symptoms (non-specific, sleep, respiratory). We found that perceived exposures were consistently associated with increased symptom scores. In general, modeled exposures except RF-EMF) were associated with increased symptom scores, but these associations disappeared or strongly diminished when perceived exposure was added in the analyses. These results indicate that perceived exposure captures an additional element of the exposure that is not captured by modeled exposure. When environmental determinants of symptoms are studied without acknowledging the potential role of exposure perceptions, there is a risk of bias in the health effects attributed to modeled exposures. By combining recent insights from both psychosocial and epidemiological research, we have highlighted a range of complex issues that previously received little attention, yet can have important implications for interpretation of epidemiological associations and public health policy and intervention strategies.

Significance Statement:

We examined modeled and perceived environmental exposures to radiofrequency electromagnetic fields (RF-EMF), noise, air pollution in relation to symptom reporting. The extent to which participants could estimate their own exposure varied, depending on the degree to which exposure sources could be observed (noise > air pollution > RF-EMF). Perceived exposures were more strongly related to self-reported symptoms, than modeled exposures. These findings show the importance of perceptions of exposures and psychosocial mechanisms for epidemiological research into environmental determinants of self-reported health. When perceptions are ignored, there is a risk of bias in the health effects attributed to modeled exposures. This has important implications for interpreting associations between environmental exposures and self-reported health and for public health policy.

1. Introduction

Radiofrequency electromagnetic fields (RF-EMF) from mobile phone base stations, noise exposure from road traffic, and air pollutants are environmental exposures often clustered in more densely populated area (1, 2). The general population is involuntarily exposed to these exposures, and many people have concerns about potential health risks. Recent studies have highlighted a complex interplay between these environmental exposures, perceptions of exposure and health risks, and symptom reporting (3–5). For example, for residential RF-EMF exposure from mobile phone base stations we recently showed that perceived, but not modeled (as a proxy for actual) exposure, was associated with self-reported symptoms (5). For noise from road traffic and air pollutants, perceptions mediated the effect of exposure on symptom-based health outcomes (3, 4). These studies show that research into environmental determinants of symptom-based health outcomes can benefit from applying insights from both psychosocial and epidemiological research disciplines.

The current study will compare effects of RF-EMF from mobile phone base stations, noise and air pollutants from road traffic for the following symptom-based health outcomes: non-specific symptoms, sleep disturbance, and respiratory symptoms. These health outcomes are chosen based on variation in the plausibility of the link with the different environmental exposures. For environmental RF-EMF exposure, there is evidence of changes in sleep electroencephalography (EEG) (6), but no convincing epidemiological evidence for specific effects on symptom-based health outcomes, nor a known biological mechanism (7, 8). However, people who regard themselves as electrohypersensitive report a wide variety of non-specific symptoms, such as headache, fatigue, and pain in numerous places which they attribute to EMF exposure (9, 10). Noise exposure on the other hand, can induce arousal, which can be observed during sleep through changes in EEG, heart rate, and respiration (11). Prior epidemiological studies reported associations between noise exposure and sleep disturbances e.g., (12–14), and there is also evidence for effects on wellbeing and an overall symptom score (15). Air pollutants can cause oxidative stress and an inflammatory response (16). Epidemiological studies have found associations between exposure to air pollutants and respiratory symptoms such as shortness of breath, coughing, and wheezing (17–19).

The expectation that negative health effects may occur, can itself induce symptoms when people think they are exposed, regardless of the actual exposure and risk (20–22). This is also described as nocebo-effect (which is the counterpart of placebo) (23). This may be a circular process, as experiencing symptoms may also influence perceptions of potential environmental health hazards (10, 24). Perceptions of environmental exposures, perceived health risks and worries play an important role in symptom experiences (25–27). The type of symptoms that are reported depends on negative expectations which may differ for example based on biological characteristics of the environmental hazard and the content of media reports (22, 28). Characteristics of a potential hazard can influence perception of health risks (29), but are also likely to influence perceptions of exposure (described as perceived exposure, or self-reported exposure). There are differences in the degree to which environmental exposures can be perceived by humans. For RF-EMF from mobile phone base stations, only the exposure source can be perceived (f.i. visibility of antennas on nearby buildings). While black smoke or diesel exhaust can sometimes be seen on windows, or smelt, there is no sensory system in humans that can directly perceive the level of air pollutants such as NO_2. Traffic noise is the only exposure, in this study, which is perceived by a specific sensory system in humans (14) and we therefore expect higher correlations with self-reported perceived exposure than for air pollutants and in particular RF-EMF.

This paper applies insights from epidemiological and psychosocial research to study environmental determinants of symptom-based health outcomes within a prospective

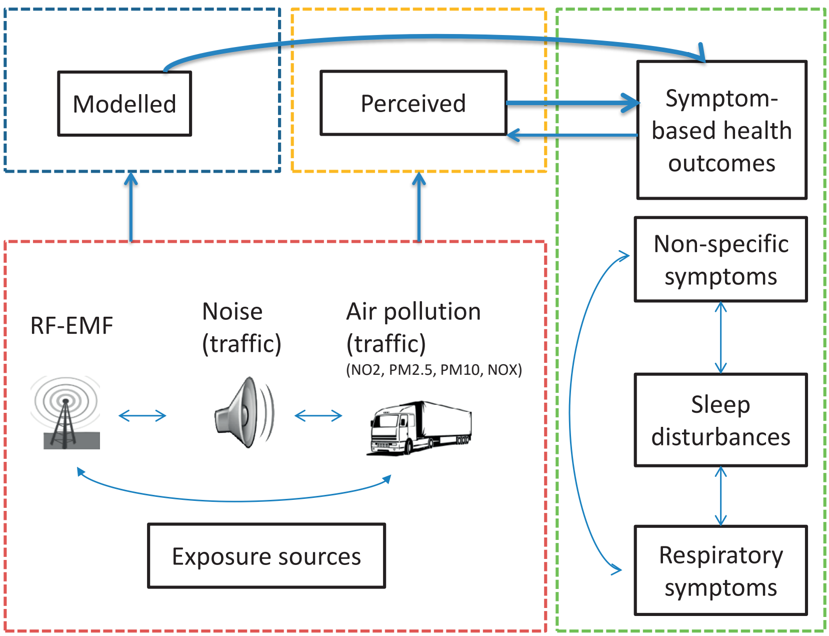

Figure 1. Analytical framework: hypothesized relations of interest between the different perceived and modeled environmental exposures (RF-EMF, noise, and air pollution) and symptom-based health outcomes (non-specific symptoms, sleep disturbances, and respiratory symptoms) in the AMIGO cohort

general population cohort (AMIGO). We have formulated three research questions, with the purpose of achieving a better understanding of the complex interplay between environmental exposures, perceptions and reported symptoms: 1) Which correlation clusters can we identify, and to what extent are there differences in correlations between modeled exposures and their corresponding perceived exposures?; 2) What are the associations between modeled exposures and symptom-based health outcomes, and between perceived exposures and symptom-based health outcomes, and how do these associations change when both modeled and perceived exposures are taken into account simultaneously?; 3) Lastly, what is the impact on perceived exposures and on health outcomes, after a change in exposures due to moving to a different home? With these final longitudinal analyses, we aim to improve our understanding of the processes that underlie the relations between modeled and perceived exposures, and symptom-based health outcomes. The hypothesized relations of interest between the different modeled and perceived urban environmental exposures (EMF, noise, and air pollutants) and symptom-based health outcomes are shown in the analytical framework in Figure 1.

2. Methods

2.1. Study population

Data for this study were collected within the Dutch population-based AMIGO cohort. This cohort was set up in 2011 and 2012 to study environmental and occupational determinants of chronic diseases and symptoms in the general population (see (46) for a full description). Participants were recruited through general practices, and were 31-65 years old at baseline (T0, 2011/2012). Of the invited 93849 people, 14829 participants responded (participation rate=16%), referred to as the baseline cohort. A follow-up questionnaire was conducted in 2015 (T1, invited n=14597, response=7905; 54%), referred to as the follow-up sample, to assess changes in exposures, exposure perceptions, and symptom-based health outcomes.

2.2. Symptom-based health outcomes

Self-reported symptom-based health outcomes (non-specific symptoms, sleep disturbances and respiratory symptoms) were assessed with the baseline and follow-up questionnaires. Non-specific symptoms were assessed with the somatization scale of the Four-Dimensional Symptom Questionnaire (4DSQ-S) (47), which consists of 16 non-specific somatic symptoms commonly reported in general practices (e.g. headaches, low back pain, and dizziness). Participants indicated for each symptom whether they were bothered by it during the previous week on a 5-point scale. The scores per symptom were trichotomized and then summed over the symptoms to obtain a total score (no=

0; sometimes= 1; regularly/often/constantly= 2). Sleep disturbances were measured with the items of the Medical Outcomes Study (MOS) (48). The sleep problem index 9 was calculated following the instructions described in (48) as a measure of overall sleep quality. Higher scores indicate more sleep disturbance, or lower sleep quality. Respiratory symptoms were assessed with items from the European Community Respiratory Health Survey II (49). A measure for respiratory symptoms is calculated as the sum of five items based on the method used by Sunyer et al. (50). A higher respiratory score indicates more respiratory symptoms.

2.3. Modeled environmental exposures

The home addresses were geocoded using data from the Netherlands Cadastre, Land Registry and Mapping Agency (Kadaster Netherlands). The geocoded home addresses were linked to various spatial models to assess (modeled) exposure at the home addresses of participants as a proxy for actual exposure. Exposures were modeled for both the baseline (2011/2012) and follow-up (2015) home addresses. For noise and air pollutants, the model estimates only changed if participants moved to a different home, as other input variables in the exposure models were not updated over time.

RF-EMF exposure from mobile phone base stations was modeled with the 3D-geospatial model NISMap. The applicability of this model for epidemiological studies has been described in a number of previous studies (52–54). The model uses detailed information about 3D building data, topography, home coordinates, bedroom elevation, antenna location, antenna characteristics and radiation patterns to compute the field strength of GSM900 (Global System for Mobile Communication), GSM1800, and UMTS (Universal Mobile Telecommunications System) frequencies at the geocoded addresses in mW/m^2. Information about location and characteristics of antennas was available for 2011, 2012, and 2014. Input data closest to the questionnaire completion date was used for the RF-EMF baseline and follow-up estimates.

Road traffic noise exposure was estimated by the Standard Model Instrumentation for Noise Assessments (STAMINA), which is a model to map environmental noise from various sources in the Netherlands (44, 55). Input variables for the calculations were noise sources (in this case only road traffic), building data, and ground type (f.i. asphalt) from the year 2011. The model takes dampening by ground and buildings into account. The resulting noise maps were linked to the coordinates of the home address. We used noise levels (dB) estimated over a whole day period (Lden), which uses penalties for the evening and night. In practice there is a very high correlation between whole day period noise estimates and night time noise estimates as shown in an earlier Dutch study (r_{Sp} of 0.99) (44). Uncertainty in the modelling of noise at low levels and lack of information on roads with low volumes of traffic led to the introduction of a cut-off value of 24 dB Lden for the noise level.

Long-term residential ambient air pollutant concentrations of NO_2 (nitrogen dioxide), NO_X (total concentration of NO and NO_2), $PM_{2.5}$ and PM_{10} (particles with an aerodynamic diameter ≤ 2.5 μm and ≤ 10 μm, respectively) were assessed using land-use regression (LUR) models developed within the European Study of Cohorts for Air Pollution Effects (ESCAPE) (41, 43), following a standardized protocol described elsewhere (41, 43) Air pollution measurements used to develop the LUR models took place between 2008 and 2011. The results section reports mainly results for NO_2, as this exposure is primarily traffic related, corresponding with our perceived exposure measure. Results for other air pollutants: NO_X, $PM_{2.5}$, PM_{10} are reported in the supplements.

2.4. Perceived environmental exposure

Perceived exposure was assessed at both time points (T0, 2011/2012 and T1, 2015) for the environmental exposures with the question: "To what extent are you exposed to: (1) electromagnetic fields/radiation from base stations for mobile phones, radio or television; (2) noise from road traffic in your home neighbourhood; (3) air pollution in the residential area from road traffic?". Answers were given on a 7-point Likert scale ranging from 0= not at all, to 6= very much.

2.5. Covariates

The baseline questionnaire included questions on sex, age (in years), highest attained level of education (classification according to Statistics Netherlands), and smoking (never, ever, current). We furthermore gathered information on neighbourhood income (percentage of income earners in the neighbourhood with an income lower than the 40th percentile of the national income distribution) as an indication of neighbourhood socioeconomic position from Statistics Netherlands (56).

2.6. Statistical analyses

We reported the baseline characteristics of the study participants and descriptives for modeled and perceived environmental exposures (RF-EMF from mobile phone base stations, noise, air pollutants), as well as the various health outcomes (non-specific symptoms, sleep disturbances, respiratory symptoms), for the two time points used in this study (T0, 2011/2012 and T1, 2015). To answer the first research question, identifying correlation clusters, Spearman correlations were calculated between all variables of interest at baseline (e.g. the correlation among all three modeled exposures, among all three perceived exposures, among the different symptom-based health outcomes, and the correlation between modeled and corresponding perceived exposure).

To address the second research question, the associations between modeled exposures, perceived exposures and the symptom-based health outcomes were analysed with mixed models. We performed both single predictor models (including modeled or perceived exposure, respectively) and two-predictor models (including modeled and perceived exposure simultaneously). We then used fixed effect models (57) in the follow-up sample to analyse temporal changes, i.e. whether intra-individual variation in perceived exposure was associated with intra-individual variation in health outcomes. Intra-individual variation in modeled exposure was not included in these fixed effect analyses, as there was no temporal (T0-T1) variation in modeled estimates for air pollutants and noise unless participants moved to a different home address (n=592).

For the last research question, to assess the impact of a change in the environment on modeled, perceived exposures and symptom-based health outcomes, we analysed only the group of participants who had moved house between baseline and follow-up and had participated in both questionnaires (n=592). Only for this group there were participants with sufficient temporal variation in modeled exposure estimates to evaluate the impact thereof on health outcomes. We first plotted the course of perceived exposure (means) over time for three percentile-based categories of absolute change (T1-T0) in modeled exposure (decrease: 0-20, no or small change: 20-80, increase: 80-100). Finally, we performed fixed effect models for the group of movers, including both modeled and perceived exposures as predictors.

Perceived and modeled exposures were analysed as continuous variables with the exception of RF-EMF from mobile phone base stations. Because of the large percentage of participants with modeled RF-EMF levels at or near 0.000 mW/m^2, we decided to dichotomize based on the 90th percentile of modeled baseline exposure, with values $\leq$ 0.050 mW/m^2 defined as low and values > 0.050 mW/m^2 defined as high, similar to Martens et. al., (2017). The health outcomes are analysed as continuous variables. All mixed models were adjusted for sex, age, education, smoking, neighbourhood income level, and for year of filling in the questionnaire (baseline/follow-up). The fixed effect model controls for all measured and unmeasured stable characteristics of an individual (57) and therefore no covariates were included in the model.

Missing values ranged between 0% and 7%. Missing values were imputed using the fully conditional method (FCS) in SAS. This method applied a discriminant function for binary/categorical variables and predictive mean matching for continuous variables. For all statistical analyses a p-value of 0.05 was used as the cut-off for statistical significance. The statistical analyses were carried out using SAS (version 9.4.; SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Descriptive statistics

Baseline characteristics of the AMIGO cohort participants at baseline (n=14829) and at the time of follow-up (n=7905) are shown in Table 1. Participants who filled in the follow-up questionnaire (follow-up sample) were more often higher educated, were less often current smokers, were on average older, and had more favorable symptom scores at baseline (Table 2) than the baseline cohort. The follow-up sample had similar scores at baseline for modeled exposures, perceived exposures and symptom scores, compared to the participants who participated only at baseline (Table 2). Over time, perceived exposures increased, and sleep disturbance and respiratory symptoms decreased in the follow-up sample. Modeled exposure values ranged from 0.00-3.13 mW/m^2 for RF-EMF, 27.00-74.80 dB for noise, and 10.25-68.39 $\mu g/m^3$ for NO_2 at baseline.

3.2. Correlations

Table 3 shows the Spearman correlations between modeled environmental exposures (RF-EMF, noise, air pollutants), perceived exposures, and symptom-based health outcomes (non-specific symptoms, sleep disturbances and respiratory symptoms). Correlation clusters were identified among the three modeled exposures (r_{Sp} 0.18-0.41), between modeled and corresponding perceived exposures (r_{Sp} RF-EMF= 0.11, noise=0.40, NO_2= 0.34), among the three perceived exposures (r_{Sp} 0.42-0.76), and the three health outcomes (r_{Sp} 0.27-0.50).

3.3. Effects of modeled and perceived exposure on symptom-based health outcomes

Table 4 summarizes the results of the mixed model analyses of all perceived and modeled exposures and the different symptom-based health outcomes (non-specific symptoms, sleep disturbances, and respiratory symptoms). Modeled RF-EMF exposure from mobile phone base stations was not significantly associated with respiratory symptoms and sleep disturbances, but was associated with lower non-specific symptom score in the single-predictor model. Perceived RF-EMF exposure was significantly associated with worse symptom-based health outcomes in all single- and two-predictor analyses.

Modeled noise exposure was significantly associated with worse scores on each symptom-based health outcome in the single-predictor models. Modeled noise exposure was associated with less sleep disturbance in the two-predictor model. Perceived noise exposure was significantly associated with worse health outcomes in all single- and two-predictor analyses.

Table 1. General baseline (2011/2012) characteristics for the baseline cohort (n=14829) and follow-up sample (n=7905) in AMIGO.

	Baseline cohort (n=14829)		Follow-up sample (n=7905)	
Variable	***n***	***%***	***n***	***%***
Sex				
Male	6 561	44.24	3 728	47.16
Female	8 268	55.76	4 177	52.84
Education				
Low	4 714	31.79	2 246	28.41
Medium	4 773	32.19	2 420	30.61
High	5 342	36.02	3 239	40.97
Smoking status				
Never	6 748	45.51	3 685	46.62
Ever	5 755	38.81	3 239	40.97
Current smoker	2 326	15.69	981	12.41
	Mean (SD)	*IQR*	*Mean (SD)*	*IQR*
age (years)	50.65 (9.37)	43.00-59.00	52.17 (9.04)	46.00-60.00
socioeconomic position (%)*	39.41 (6.92)	35.00-44.00	39.16 (6.87)	34.00-44.00

* Percentage income-earners with a low-income in the neighbourhood.

Table 2. Exposure and health outcome characteristics for the baseline AMIGO cohort (n=14829) at T0 (2011/2012) and for the follow-up sample (n=7905) at T0 (2011/2012) and T1 (2015).

	Baseline cohort T0 (n=14829)		Follow-up sample T0 (n=7905)		Follow-up sample T1 (n=7905)	
Variable	**Mean (SD)**	**IQR**	**Mean (SD)**	**IQR**	**Mean (SD)**	**IQR**
modeled RF-EMF (mW/m^2)	0.02 (0.09)	0.00-0.01	0.02 (0.09)	0.00-0.01	0.03 (0.11)	0.00-0.02
modeled Noise (dB)	53.11 (5.82)	49.40-56.70	53.15 (5.86)	49.40-56.70	53.14 (5.86)	49.40-56.70
modeled NO_2 (μg/m^3)	22.11 (5.60)	18.30-25.53	22.22 (5.59)	18.44-25.64	22.19 (5.60)	18.38-25.61
perceived Base station (0-6)	1.05 (1.26)	0.00-2.00	1.02 (1.21)	0.00-2.00	1.22 (1.45)	0.00-2.00
perceived Noise (0-6)	1.65 (1.48)	1.00-2.00	1.62 (1.44)	1.00-2.00	1.96 (1.58)	1.00-3.00
perceived Air pollution (0-6)	1.83 (1.55)	1.00-3.00	1.82 (1.52)	1.00-3.00	2.17 (1.64)	1.00-3.00
Non-specific symptoms (0-32)	5.96 (5.24)	2.00-8.00	5.66 (5.00)	2.00-8.00	5.64 (4.93)	2.00-8.00
Sleep disturbances (0-100)	27.18 (14.71)	16.11-35.56	26.42 (14.28)	15.56-33.89	25.40 (14.26)	15.56-33.33
Respiratory symptoms (0-5)	0.48 (0.97)	0.00-1.00	0.44 (0.91)	0.00-1.00	0.40 (0.87)	0.00-0.00

SD=standard deviation, IQR=interquartile range, RF-EMF=radiofrequency electromagnetic fields, NO_2=nitrogen dioxide.

Table 3. Spearman correlation coefficients for modeled exposures, perceived exposure and symptom-based health outcomes in the AMIGO baseline cohort (n=14829, T0 = 2011/2012).

		Modeled exposure			Perceived exposure			Symptom-based health outcomes		
		RF-EMF (mW/m^2)	Noise (dB)	NO_2 (µg/m^3)	Base station	Noise	Air pollution	Non-specific symptoms	Sleep disturbances	Respiratory symptoms
Modeled exposure	RF-EMF (mW/m^2)									
	Noise (dB)	0.18								
	NO_2 (µg/m^3)	0.39	0.41							
Perceived exposure	Base station	0.11	0.11	0.15						
	Noise	0.14	0.40	0.28	0.42					
	Air pollution	0.15	0.35	0.34	0.46	0.76				
Symptom-based health outcomes	Non-specific symptoms	0.03	0.03	0.05	0.10	0.12	0.10			
	Sleep disturbances	0.03	0.03	0.06	0.13	0.14	0.12	0.50		
	Respiratory symptoms	0.03	0.03	0.05	0.06	0.07	0.08	0.37	0.27	

RF-EMF=radiofrequency electromagnetic fields, NO_2=nitrogen dioxide.
Darker colors indicate higher correlations.

Modeled NO_2 was significantly associated with worse scores on each symptom-based health outcomes in the single predictor models and in the two-predictor models, although effects of NO_2 diminished when perceived exposure was included in the two-predictor model. Perceived exposure to air pollution from road traffic was significantly associated with worse health outcomes in all single- and two-predictor analyses. Results for NO_x, $PM_{2.5}$, and PM_{10} were similar (Supplement Table S1), although the majority of the associations for these modeled air pollutants were not significant in the two-predictor models.

Table 4. Mixed model analyses of Modeled and Perceived Exposure to RF-EMF from Mobile Phone Base Stations, Traffic Noise and Road Traffic Air Pollution on **Non-specific symptoms**, **Sleep disturbances**, and **Respiratory symptoms** for AMIGO respondents (n=14829, T0 = 2011/2012 and n=7905, T1=2015).

		Non-specific symptoms (0-32)		Sleep disturbances (0-100)		Respiratory symptoms (0-5)	
		β (95%CI)*	p	β (95%CI)*	p	β (95%CI)*	p
RF-EMF							
1	modeled (0-1)	-0.23 (-0.43,-0.03)	0.026[a]	-0.58 (-1.15,0.00)	0.051	-0.03 (-0.07,0.01)	0.096
2	perceived (0-6)	**0.37 (0.32,0.40)**	**0.000**	**0.81 (0.68,0.94)**	**0.000**	**0.04 (0.03,0.05)**	**0.000**
3	modeled (0-1)	-0.13 (-0.33,0.07)	0.201	-0.36 (-0.94,0.22)	0.222	-0.02 (-0.06,0.02)	0.305
	perceived (0-6)	**0.37 (0.32,0.41)**	**0.000**	**0.80(0.67,0.93)**	**0.000**	**0.04 (0.03,0.05)**	**0.000**
Noise							
1	modeled (dB)	**0.02 (0.01,0.03)**	**0.001**	**0.05 (0.01,0.09)**	**0.008**	**0.00 (0.00,0.01)**	**0.002**
2	perceived (0-6)	**0.30 (0.26,0.35)**	**0.000**	**0.83 (0.72,0.95)**	**0.000**	**0.04 (0.03,0.05)**	**0.000**
3	modeled (dB)	-0.01 (-0.03,0.00)	0.067	-0.04 (-0.08,-0.00)	0.028[a]	-0.00 (-0.00,0.00)	0.655
	perceived (0-6)	**0.32 (0.28,0.36)**	**0.000**	**0.88 (0.76,1.01)**	**0.000**	**0.04 (0.03,0.05)**	**0.000**
NO_2							
1	modeled (µg/m^3)	**0.05 (0.04,0.06)**	**0.000**	**0.15 (0.11,0.19)**	**0.000**	**0.01 (0.01,0.01)**	**0.000**
2	perceived (0-6)	**0.27 (0.23,0.31)**	**0.000**	**0.67 (0.56,0.78)**	**0.000**	**0.04 (0.03,0.05)**	**0.000**
3	modeled (µg/m^3)	**0.02 (0.01,0.04)**	**0.001**	**0.10 (0.05,0.14)**	**0.000**	**0.00 (0.00,0.01)**	**0.000**
	perceived (0-6)	**0.25 (0.21,0.29)**	**0.000**	**0.59 (0.48,0.71)**	**0.000**	**0.04 (0.03,0.06)**	**0.000**

1. These are the single predictor models for modeled exposure. 2. These are the single predictor models for perceived exposure. 3. These are the two-predictor models, i.e. including both modeled and perceived exposure.

*Adjusted for baseline values of sex, age, education, smoking, socioeconomic position, and year (baseline/follow-up).

RF-EMF=radiofrequency electromagnetic fields, PM= particulate matter, NO_2=nitrogen dioxide.

Adverse effects are printed in bold if the p-value is lower than 0.05.

[a] beneficial effects with p-value below 0.05

Table 5 summarizes the results of the fixed effect analyses in which temporal changes on an individual basis (between T0 and T1) in perceived exposure were related to changes in symptom reporting for the follow-up sample (n=7905). For all environmental exposures, changes in perceived exposure were significantly associated with corresponding change in non-specific symptoms. Change in perceived RF-EMF exposure from base stations and noise exposure was significantly associated with a corresponding change in sleep disturbance. Change in perceived air pollution from road traffic was significantly associated with a corresponding change in respiratory symptoms.

Table 5. Fixed effect analyses for effects of intra-individual changes in Perceived Exposure to Mobile Phone Base Stations, Noise and Air Pollution on intra-individual changes in **Non-specific symptoms**, **Sleep disturbances**, and **Respiratory symptoms** for AMIGO respondents (n=7905) who participated at T0 (2011/2012) and T1 (2015).

	Non-specific symptoms (0-32)		Sleep disturbances (0-100)		Respiratory symptoms (0-5)	
	B (95%CI)*	p	B (95%CI)*	p	B (95%CI)*	p
Perceived Base station (0-6)	**0.16 (0.10, 0.22)**	**0.000**	**0.19 (0.01, 0.36)**	**0.042**	0.01 (-0.00,0.02)	0.161
Perceived Noise (0-6)	**0.07 (0.01, 0.13)**	**0.021**	**0.21 (0.03, 0.39)**	**0.019**	0.01 (-0.01,0.02)	0.311
Perceived Air pollution (0-6)	0.04 (0.02, 0.10)	0.184	0.08 (-0.09, 0.25)	0.344	**0.01 (0.00,0.03)**	**0.049**

Adverse effects are printed in bold if the p-value is lower than 0.05.

3.4. Effects of a change of environment

In total 1224 (8.25%) participants moved to a different home address between baseline in 2011/2012 (T0) and the follow-up questionnaire in 2015 (T1); of these, 592 participants filled in both questionnaires. This change of environment sometimes resulted in changed modeled and perceived exposures. Moved participants were categorized into three percentile based categories of change in absolute modeled exposure (decrease: 0-20 percentile, no change: 20-80, increase: 80-100). The cut-off points of the categories for the absolute change in modeled exposure are presented in Supplement Table S2. Figure 2 presents the course of mean perceived exposures over time for these three categories. For the group of participants with an increase in modeled exposure, the corresponding average perceived exposure increased as well in the same time period, in particular for NO_2 and noise. For the participants with a decrease in modeled exposure, the corresponding average perceived exposure decreased as well over time for noise and NO_2, but not for RF-EMF, which remained the same. Supplement Table S3 shows that intra-individual variation in perceived exposures and modeled exposures were not significantly associated with any intra-individual variation in symptom-based

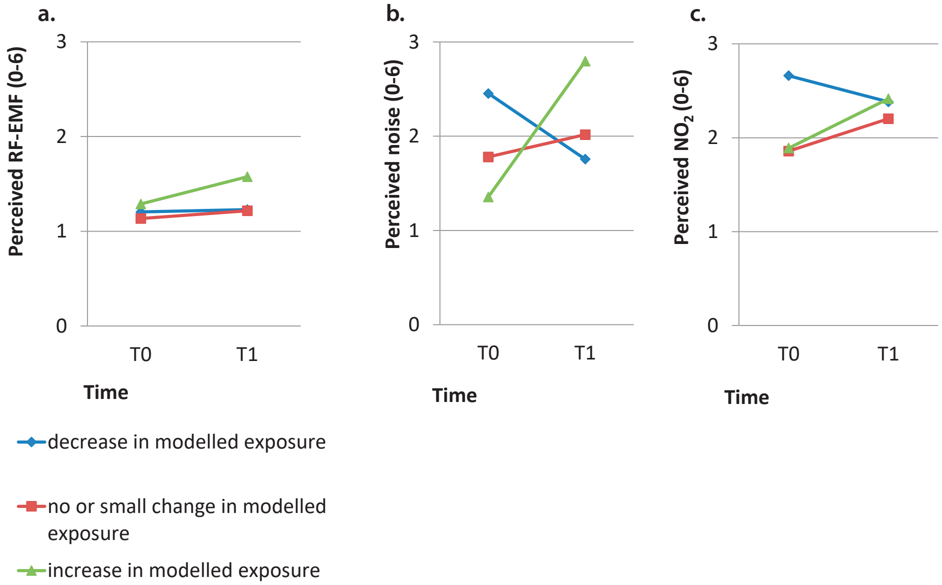

Figure 2. Course of mean perceived exposures (a= RF-EMF, b =Noise, c= NO_2) over time (T0 =2011/2012, T1 = 2015) for AMIGO respondents who moved house between T0 and T1 (n=592) for percentile based categories (0-20, 20-80, 80-100) of absolute change in the corresponding modeled exposure.

* For each exposure (a=RF-EMF, B=noise, c=NO_2), moved participants were divided in three percentile based categories (decrease: 0-20, no or small change in modeled exposure: 20-80, increase: 80-100) of the absolute change in modeled exposure between baseline and follow-up (see supplement table S3).

RF-EMF=radiofrequency electromagnetic fields and NO_2=nitrogen dioxide.

health outcomes, except for perceived RF-EMF, which was significantly associated with intra-individual variation in non-specific symptoms and sleep disturbance.

4. Discussion

In this prospective cohort study, we examined the interplay between three modeled and perceived environmental exposures (RF-EMF from mobile phone base stations, noise and air pollutants from road traffic) and three symptom-based health outcomes (non-specific symptoms, sleep disturbances, and respiratory symptoms).

4.1. Interpretation results

Correlation clusters

First, we found substantial correlation clusters among the three modeled exposures, the three perceived exposures and three different symptom-based health outcomes. Further, it seems that beliefs of participants about their exposure level to noise and air pollutants corresponded to some extent with their modeled exposure level, whereas this was not apparent for RF-EMF. In line with previous work (5), we found low correlations between modeled and perceived exposure to RF-EMF from mobile phone base stations. The low levels of knowledge regarding RF-EMF in the general population (30) likely plays a role. An additional factor is that RF-EMF exposure cannot be perceived directly by a sensory system, while noise and in part air pollution exposure can (14). As expected, we found much higher correlations between modeled and perceived exposure for noise exposure from traffic (1). For air pollution from road traffic, correlations between modeled and perceived exposure were only slightly lower than for noise exposure. Perhaps familiarity with the link between road traffic and air pollutants, the visibility of nearby roads and the smell of exhaust gave participant an indication of the level of air pollutants near the home. As expected, we found correlations among modeled exposures, likely due to the clustering of exposures in urbanized areas. Correlation clusters among perceived exposures could be explained by a general environmental health worry factor (31), as well as the clustering of actual exposures. Correlations among health outcomes may be partly explained by underlying factor, representing a general tendency to report symptoms (32). The presence of substantial correlation clusters among modeled exposures, perceived exposures, and health outcomes, implicates that disentanglement of different exposures and their individual health effects may prove difficult in epidemiological research.

Effects of modeled and perceived exposure on symptom-based health outcomes

Modeled RF-EMF was not associated with higher symptom scores, which is in line with earlier conducted studies (5, 33, 34). For modeled noise exposure, prior studies on self-reported health (12–14) indicated that noise is mainly associated with increased sleep disturbances, and air pollutants mainly with respiratory symptoms (17–19). The results of single predictor models in this study confirm the presence of significant adverse effects of noise and air pollutants on symptom scores. Contrary to our expectations, these health effects extended across all assessed health outcomes, even those not previously reported in literature. However, the results were notably different in the two-predictor models, that included both modeled and perceived exposures. Significant adverse effects of modeled exposures on health outcomes generally disappeared (noise) or severely diminished (NO_2), when perceived exposure was included in the model. In two analyses (Table 4: effect of RF-EMF on non-specific symptoms, effect of noise on sleep disturbance) we found unexpected beneficial effects of modeled exposures, but these effects were small and possibly coincidental findings. The associations with symptom scores indicate a greater maximum impact of perceived than modeled exposure on symptom scores, for both single- and two-predictor models (as is shown in Supplementary Table S4). These findings indicate that perceptions of exposures can play an important role when studying environmental determinants of symptom-based health outcomes.

High scores on perceived exposures are likely to be in part the result of features of the environment that also drive modeled exposure levels (such as the proximity of nearby roads). In addition, worries about potential health effects of the specific exposure, and worries about environmental risks in general (25), can influence perceived exposure scores. A part of the cohort participants moved to a new home (n=592), and therefore changed their residential environment which affected their modeled exposure levels. For this group, we found that a substantial increase or decrease in modeled exposure with respect to noise and air pollution (NO_2) was coupled with a simultaneous increase, respectively decrease in the corresponding perceived exposure (Figure 2). This longitudinal evidence strengthens the conclusion that participants are to some extent aware of, and able to estimate, the level of these two environmental exposures in their residential environment. The observed relation with change in perception was less distinct for RF-EMF from mobile phone base stations. Here, risk perception and health concerns appear to influence perceived exposure to a greater extent than exposure cues such as visibility of nearby base stations.

In the group of follow-up participants (n=7905), change in perceived exposures was significantly positively associated with change in most symptom-based health outcomes in the fixed effect analyses. This finding was not replicated in the smaller group of moved participants (n=592), except for positive effects of change in perceived RF-EMF on change in non-specific symptoms and sleep disturbance. However, due to the small number of movers, the power to detect such associations was limited in this subgroup. A change in perceived exposure in a new residential environment can be important given the associations between higher exposure perception and increased symptom scores, which were in line with earlier studies (3, 4, 35, 36).

The implications of these findings in combination with the role of modeled exposures depend on the underlying causal mechanisms. The framework with the hypothesized relationships between the variables we assessed in this study is shown in figure 1. A causal link from the exposure source both to modeled exposure (as a proxy of the true exposure level) and to perceived exposure is plausible(37), based on observability of exposure sources, and supported by the results of this study. For exposures that can be sensorially observed (f.i. noise) sensitivity and annoyance can play role as mediator (4) in the association between perceived exposure and symptom scores. In addition, there is sufficient evidence for the existence of nocebo effects (20, 22, 38), to support a causal link between perceived exposure and reported symptoms through negative health expectations when participants think they are exposed. If such nocebo effects occur in this population, mediation effects of modeled exposure on symptom scores through perceived exposure would be likely. Such mediation mechanisms can have an impact on epidemiological studies examining environmental determinants of symptom-based health outcomes. When perceived exposure is not taken into account, indirect health effects through perceived exposure may be incorrectly ascribed to modeled environmental exposures. However, the importance of such mediation mechanisms could be overestimated. Nocebo mechanisms have been mainly studied in laboratory and field-experiment studies, but the extent to which they are important for associations between perceived exposures and reported symptoms in the general population is unknown. Mechanisms of reversed causation may also play a role. For example, participants with health problems with an unknown cause may become more aware of environmental exposures in their environment, and incorrectly start attributing these to environmental sources (10, 39, 40). They experience and report their perceived exposure levels differently than healthy participants, which often is described as recall bias in epidemiological research and can be a problem in cross-sectional research and case-control studies. In this longitudinal study, with the use of a qualitative measure of perceived exposure, that is intended to capture the subjective experience of self-reported exposure, it perhaps is better described as a process of reversed causation. Depending on characteristics of the individual, but also features of the environment, such as recent changes in exposure versus a stable situation, different processes underlying causal mechanisms of the link between exposure perceptions and symptom experiences could be important. Clarifying the underlying mechanisms is of great interest and importance for both epidemiological and psychosocial research disciplines, because of the implications for the interpretation of the relationships between the environment, perception, and symptom experiences. In addition, the need for effective public health intervention measures and policy implications varies depending on the importance of different mechanisms. Intervention measures targeted at reducing negative health expectations will only be effective in reducing symptom scores if the nocebo mechanism is the main explanation for the associations between exposure perception and reported symptoms.

4.2. Strengths and Limitations

The study had a large study sample for studying the symptom-based health outcomes of interest. In addition, there were observations at two points in time, allowing for longitudinal analyses for a subset of participants. Thirdly, all studied exposures were modeled using validated geospatial models that have been used in previous epidemiological research (41–44). These models do not require manual data-collection, allowing for research in large country-wide cohort studies. A limitation of the current study was that we only had modeled estimates for noise and air pollutants for one point in time (i.e. baseline), because input data for the models was not available for different years. Although estimates for noise and air pollutants would have improved slightly with new input data, large changes in exposure are not expected in this relatively short time frame. Eeftens et. al. (2011) showed that NO_2 decreased only slightly between 1997 and 2007 and correlations were high (45). Another limitation concerns RF-EMF, where we modeled exposure from mobile phone base stations while perceived exposure also included radio and tv base stations, because we expected people to not be familiar with differences between mobile phone and radio/tv base stations. However, given that mobile phone base stations are by far more present in residential areas, we expect this to dominate perceived RF-EMF levels.

4.3. Conclusion

Our study covered three environmental exposures, both modeled and perceived, and three symptom-based health outcomes. Correlations between modeled and perceived exposures appeared to be influenced by the observability of the exposure sources. Due to correlation clusters among modeled and perceived exposures, and among health outcomes, disentangling the effects of individual environmental exposures on health is a methodological challenge. Perceived exposures were consistently associated with increased symptom scores. In general, modeled exposures (except RF-EMF) were associated with increased symptom scores, but these associations disappeared or strongly diminished when perceived exposure was also added as a predictor. Under the reasonable assumption that perceived exposure is not a better proxy of the actual exposure than modeled exposure, these results would indicate that perceived exposure captures an additional element of the exposure that is not captured by the modeled exposure. When environmental determinants of symptoms are studied without acknowledging the potential role of these exposure perceptions, there is a risk of biasing the health effects attributed to modeled exposures. However, the etiological role of exposure perceptions in relation to symptom reporting requires further research. By combining insights from epidemiological and psychosocial research we have highlighted a range of complex issues that previously received little attention, but which can have important implications for interpretation of associations of interest, public health policy and intervention strategies.

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Supplementary tables

Table S1. Mixed model analyses of Modeled and Perceived Exposure to Air pollutants (NO_2, NO_X, $PM_{2.5}$, PM_{10}) on **Non-specific symptoms**, **Sleep disturbances**, and **Respiratory symptoms** for AMIGO respondents (n=14829, T0 = 2011/2012 and n=7905, T1=2015).

		Non-specific symptoms (0-32)		Sleep disturbances (0-100)		Respiratory symptoms (0-5)	
		β (95%CI)*	p	β (95%CI)*	p	β (95%CI)*	p
NO_2							
1	modeled (μg/m³)	**0.05 (0.04,0.06)**	**0.000**	**0.15 (0.11,0.19)**	**0.000**	**0.01 (0.01,0.01)**	**0.000**
2	perceived (0-6)	**0.27 (0.23,0.31)**	**0.000**	**0.67 (0.56,0.78)**	**0.000**	**0.04 (0.03,0.05)**	**0.000**
3	modeled (μg/m³)	**0.02 (0.01,0.04)**	**0.001**	**0.10 (0.05,0.14)**	**0.000**	**0.00 (0.00,0.01)**	**0.000**
	perceived (0-6)	**0.25 (0.21,0.29)**	**0.000**	**0.59 (0.48,0.71)**	**0.000**	**0.04 (0.03,0.06)**	**0.000**
NO_x							
1	modeled (μg/m³)	**0.02 (0.01,0.03)**	**0.000**	**0.05 (0.03,0.07)**	**0.000**	**0.00 (0.00,0.01)**	**0.000**
2	perceived (0-6)	**0.27 (0.23,0.31)**	**0.000**	**0.67 (0.56,0.78)**	**0.000**	**0.04 (0.03,0.05)**	**0.000**
3	modeled (μg/m³)	0.01 (-0.00,0.01)	0.153	0.01 (-0.01,0.04)	0.236	0.00 (-0.00,0.00)	0.068
	perceived (0-6)	**0.26 (0.22,0.30)**	**0.000**	**0.65 (0.53,0.77)**	**0.000**	**0.04 (0.03,0.05)**	**0.000**
$PM_{2.5}$							
1	modeled (μg/m³)	**0.20 (0.09,0.32)**	**0.001**	**0.59 (0.26,0.92)**	**0.000**	**0.02 (0.00,0.04)**	**0.041**
2	perceived (0-6)	**0.27 (0.23,0.31)**	**0.000**	**0.67 (0.56,0.78)**	**0.000**	**0.04 (0.03,0.05)**	**0.000**
3	modeled (μg/m³)	0.08(-0.04,0.19)	0.197	0.28 (-0.05,0.61)	0.096	0.00 (-0.02,0.02)	0.870
	perceived (0-6)	**0.27 (0.23,0.31)**	**0.000**	**0.66 (0.54,0.77)**	**0.000**	**0.04 (0.03,0.05)**	**0.000**
PM_{10}							
1	modeled (μg/m³)	**0.24 (0.16,0.32)**	**0.000**	**0.63 (0.40,0.86)**	**0.000**	**0.04 (0.02,0.05)**	**0.000**
2	perceived (0-6)	**0.27 (0.23,0.31)**	**0.000**	**0.67 (0.56,0.78)**	**0.000**	**0.04 (0.03,0.05)**	**0.000**
3	modeled (μg/m³)	0.08 (-0.00,0.17)	0.056	**0.25 (0.01,0.49)**	**0.044**	0.01 (-0.00,0.03)	0.117
	perceived (0-6)	**0.26 (0.22,0.30)**	**0.000**	**0.64 (0.52,0.75)**	**0.000**	**0.04 (0.03,0.05)**	**0.000**

1. These are the single predictor models for modeled exposure. 2. These are the single predictor models for perceived exposure. 3. These are the two-predictor models, i.e. including both modeled and perceived exposure.
*Adjusted for baseline values of sex, age, education, smoking, socioeconomic position, and year.
NO_2=nitrogen dioxide, NO_x = nitrogen oxide and PM=particulate matter.
Adverse effects are printed in bold if the p-value is lower than 0.05.

Table S2. Mean, minimum and maximum absolute change in modeled exposures for the different percentile based categories (0-20, 20-80, 80-100) for AMIGO respondents (n=592) who moved to a different home address between T0 (2011/2012) and T1 (2015).

Exposure	Mean absolute change for each category	Minimum absolute change for each category	Maximum absolute change for each category
RF-EMF (mW/m^2)			
Decrease (percentile 0-20)	-0.078	-0.870	-0.010
No or small change (percentile 20-80)	0.003	-0.010	0.0280
Increase (percentile 80-100)	0.157	0.0290	1.417
Noise (dB)			
Decrease (percentile 0-20)	-10.308	-24.780	-6.100
No or small change (percentile 20-80)	-0.047	-6.100	5.400
Increase (percentile 80-100)	9.686	5.400	20.500
NO_2 (µg/m^3)			
Decrease (percentile 0-20)	-7.859	-27.382	-4.081
No or small change (percentile 20-80)	-0.371	-4.050	2.756
Increase (percentile 80-100)	6.872	2.770	31.779

RF-EMF=radiofrequency electromagnetic fields and NO_2=nitrogen dioxide

Table S3. Fixed effect analyses of effects of Modeled and Perceived Exposure to Mobile Phone Base Stations, Noise and Air Pollution on **Non-specific symptoms**, **Sleep disturbances**, and **Respiratory symptoms** for AMIGO respondents (n=592) that moved between baseline (2011/2012) and follow-up (2015) questionnaire.

		Non-specific symptoms (0-32)		Sleep disturbances (0-100)		Respiratory symptoms (0-5)	
		β (95%CI)*	p	β (95%CI) *	p	β (95%CI) *	p
RF-EMF	Modeled (0-1)	0.42 (-0.26,1.11)	0.226	-0.03 (-2.05,1.99)	0.977	0.09 (-0.06,0.25)	0.237
	Perceived (0-6)	**0.30 (0.08,0.52)**	**0.008**	**0.71 (0.05,1.36)**	**0.034**	-0.00 (-0.05,0.05)	0.893
Noise	Modeled (dB)	-0.04 (-0.09,0.01)	0.100	-0.13 (-0.28,0.01)	0.074	-0.00 (-0.01,0.01)	0.526
	Perceived (0-6)	-0.03 (-0.22,0.16)	0.735	0.03 (-0.52,0.59)	0.902	-0.01 (-0.05,0.04)	0.777
NO_2	Modeled (μg/m^3)	-0.07 (-0.13,-0.01)	0.029[a]	-0.16 (-0.34,0.02)	0.079	-0.00 (-0.02,0.01)	0.499
	Perceived (0-6)	-0.08 (-0.27,0.11)	0.394	0.24 (-0.31,0.79)	0.394	-0.01 (-0.04,0.04)	0.926
NO_x	Modeled (μg/m^3)	-0.01 (-0.04,0.02)	0.548	-0.04 (-0.13,0.04)	0.306	0.00 (-0.00,0.01)	0.517
	Perceived (0-6)	-0.11 (-0.30,0.08)	0.262	0.21 (-0.35,0.76)	0.466	-0.01 (-0.05,0.03)	0.739
$PM_{2.5}$	Modeled (μg/m^3)	0.19 (-0.43,0.82)	0.541	-0.14 (-1.98,1.70)	0.880	-0.07 (-0.21,0.07)	0.311
	Perceived (0-6)	-0.13 (-0.32,0.06)	0.176	0.16 (-0.40,0.72)	0.571	-0.00 (-0.04,0.04)	0.995
PM_{10}	Modeled (μg/m^3)	-0.10 (-0.40,0.20)	0.519	-0.61 (-1.49,0.28)	0.180	-0.00 (-0.07,0.07)	0.992
	Perceived (0-6)	-0.10 (-0.29,0.09)	0.282	0.24 (-0.32,0.80)	0.402	-0.00 (-0.05,0.04)	0.835

RF-EMF=radiofrequency electromagnetic fields, NO_2=nitrogen dioxide, NO_x = nitrogen oxide and PM= particulate matter.
Adverse effects are printed in bold if the p-value is lower than 0.05.
[a] beneficial effects with p-value below 0.05

Table S4. Comparison of effect sizes based on the Mixed effect model analyses of Modeled and Perceived Exposure to RF-EMF from Mobile Phone Base Stations, Traffic Noise and Road Traffic Air Pollution on **Non-specific symptoms**, **Sleep disturbances**, and **Respiratory symptoms** for AMI-GO respondents (n=14829, T0 = 2011/2012 and n=7905, T1=2015).

		Non-specific symptoms (0-32)	Sleep disturbances (0-100)	Respiratory symptoms (0-5)
	Predictors	maximum modeled effect on symptoms (maximum effect as percentage of the baseline mean)		
RF-EMF				
1	modeled (0-1)	-0.23 (-3.9%)	-0.58 (-2.1%)	-0.033 (-7.1%)
2	perceived (0-6)	2.21 (37.2%)	4.84 (17.8%)	0.042 (8.9%)
3	modeled (0-1)	-0.13 (-2.2%)	-0.36 (-1.3%)	-0.021 (-4.4%)
	perceived (0-6)	2.20 (37.0%)	4.81 (17.7%)	0.042 (8.9%)
Noise				
1	modeled (dB)	0.49 (8.2%)	1.16 (4.3%)	0.004 (0.8%)
2	perceived (0-6)	1.83 (30.8%)	5.00 (18.4%)	0.040 (8.6%)
3	modeled (dB)	-0.30 (-5.0%)	-1.01 (-3.7%)	-0.001 (-0.1%)
	perceived (0-6)	1.91 (32.2%)	5.29 (19.5%)	0.041 (8.7%)
NO_2				
1	modeled ($\mu g/m^3$)	1.09 (18.4%)	3.39 (12.5%)	0.009 (1.8%)
2	perceived (0-6)	1.62 (27.3%)	4.03 (14.8%)	0.043 (9.0%)
3	modeled ($\mu g/m^3$)	0.55 (9.2%)	2.10 (7.7%)	0.005 (1.0%)
	perceived (0-6)	1.50 (25.3%)	3.56 (13.1%)	0.038 (8.1%)
No_x				
1	modeled ($\mu g/m^3$)	0.82 (13.8%)	2.01 (7.4%)	0.004 (0.8%)
2	perceived (0-6)	1.62 (27.3%)	4.03 (14.8%)	0.043 (9.0%)
3	modeled ($\mu g/m^3$)	0.24 (4.0%)	0.55 (2.0%)	0.001 (0.3%)
	perceived (0-6)	1.57 (26.5%)	3.91 (14.4%)	0.040 (8.5%)
$PM_{2.5}$				
1	modeled ($\mu g/m^3$)	0.48 (8.1%)	1.40 (5.1%)	0.022 (4.6%)
2	perceived (0-6)	1.62 (27.3%)	4.03 (14.8%)	0.043 (9.0%)
3	modeled ($\mu g/m^3$)	0.18 (3.0%)	0.66 (2.4%)	0.002 (0.4%)
	perceived (0-6)	1.60 (26.9%)	3.93 (14.5%)	0.042 (9.0%)

Table S4. (*continued*)

		Non-specific symptoms (0-32)	Sleep disturbances (0-100)	Respiratory symptoms (0-5)
PM_{10}				
1	modeled (µg/m^3)	0.83 (14.0%)	2.19 (8.1%)	0.037 (7.9%)
2	perceived (0-6)	1.62 (27.3%)	4.03 (14.8%)	0.043 (9.0%)
3	modeled (µg/m^3)	0.29 (4.8%)	0.85 (3.1%)	0.012 (2.7%)
	perceived (0-6)	1.55 (26.1%)	3.81 (14.0%)	0.040 (8.6%)

The maximum impact of the predictors on symptom scores was calculated by multiplying the range of the predictor values with the regression coefficients. The percentage in brackets represents the maximum impact of the predictors as a percentage of the mean symptom score at baseline. RF-EMF=radiofrequency electromagnetic fields, NO_2=nitrogen dioxide, NO_x = nitrogen oxide and PM= particulate matter. * For continuous predictors the range was calculated as the 97.5th percentile minus the 2.5th percentile to exclude impact of extreme values.

General discussion

8

8.0. General discussion

The introduction of mobile phone base stations in the society has led to concerns about the potential health effects of this new exposure among citizens (1) and scientists (2). The aim of this thesis was to improve the understanding of the associations between modelled (as a proxy of actual) and perceived exposure to RF-EMF from mobile phone base stations in relation to self-reported health outcomes. The findings showed that perceptions of exposure to RF-EMF from mobile phone base stations, and perceptions of health risks, play an important role in self-reported health outcomes, in contrast to modelled exposure. Through the application of recent insights from epidemiological and psychosocial research in a longitudinal research design, this thesis contributed to advancing the knowledge in this field. This chapter will discuss the overall findings, ongoing developments, and the impact for research and society.

8.1. Exposure assessment

This thesis addressed the challenging task of characterizing an individual's RF-EMF exposure from mobile phone base stations in epidemiological studies. Geospatial model (NISMap) predictions at the home address were compared with personal measurements in two separate studies (3, 4). The results showed that modelling exposure at the home address is a suitable method for exposure assessment in epidemiological studies. The impact of participants' mobility on the accuracy of the model estimations was limited. However, there was still substantial misclassification. As high exposure levels are rare, misclassification is potentially problematic because epidemiological studies then need a very large sample size to have sufficient power to detect health effects, especially when the studied health outcome is rare, or the potential health effect is very small (5). In this thesis exposure misclassification probably did not impede the results of the study to a great extent, as the studied health issues (self-reported symptoms) were common and the sample relatively large (almost 15000 participants from the AMIGO cohort (6), in 2011 and 2012). Modelling exposure, rather than measuring, has advantages for epidemiological research because an increase in the number of participants does not come with a linear cost increase.

Further improvements in exposure assessment would aid future epidemiological studies. Improvements may be achieved by improvements in the accuracy of model input data, such as more accurate 3D building data and information about the location and characteristics of antenna's (7, 8). In the future, modelling far field RF-EMF exposure may become more challenging, as there is an ongoing change in technology use from the application of large macro stations to more micro stations and femtocells (9). The output power of these stations is lower, but the number needed for adequate mobile phone service is much larger, and it may be more difficult to gather accurate input data for model estimations. New technologies may also offer opportunities for improved exposure assessment. The location of study participants can be continuously tracked through their mobile phone (10, 11). Then, exposure is modelled not only at the home address, but at every location the participant has spent some time (for example at work, or visiting a friend), potentially leading to improvement in the accuracy of exposure assessment. The use of this method is not likely to lead to huge gains, given the limited impact of time spent outside the home on the accuracy of the model estimations in this thesis. However, more substantial improvements in accuracy may be achieved for participant groups who spend more time outside the home than participants in our measurement studies (chapter 2 & 3). When such methods are applied, there should be ethical discussions about the privacy implications of such methods, as proper anonymization of individual data may not always be possible (12). Ethical considerations are important in particular when this method is applied in combination with adaptive health tracking, for example by requesting participants to fill in questions about their health when their exposure is above a certain level (11). Invited participants may feel uncomfortable with this type of data collection and refuse to participate, although recruiting participants was not a problem in a recent study that applied this method (11). Low participation rates are a major problem in many recent studies, lowering the generalizability of the findings. On the other hand, mobile phone technology may provide opportunities to improve recruitment of demographic groups that are currently often underrepresented in questionnaire based research, such as younger participants, participants with a lower socioeconomic position and ethnic minorities (11, 13). These demographic groups were also underrepresented in the AMIGO cohort.

8.2. Risk appraisal and Attribution

Previous studies have shown that perceptions of environmental exposures and health risks can play a role in symptom reporting (14–16). In this study, a minority of the participants indicated that they were thought they were exposed to RF-EMF from mobile phone base stations (AMIGO cohort 2011/2012, mean = 1.0, SD= 1.2, on a scale of 0-6) or that exposure could be a health risk (AMIGO cohort 2011/2012, mean = 1.3, SD= 1.5, on a scale of 0-6). In previous studies in the Netherlands (17, 18) and other countries (1, 19–22) participants often reported relatively higher scores on measures of perceived exposure, perceived risk, or concerns regarding health risks of EMF. Different factors may have played a role, for example the recruitment strategy. The number of participants who are concerned about EMF may be higher when health risks of EMF or other technologies are an explicit focus of invitation letters to participate in research. Also, cultural and social factors, including alarming media reports (23) can influence the public perception of EMF risks and lead to different perceptions in different countries.

Although the perception of mobile phone base stations was not as negative as in some other studies, the portion of the population with high risk appraisal was still substantial. High risk appraisal is related to lower trust in the responsible authorities (18), and risk appraisal can also be a factor in protest actions against the placement of new mobile phone base stations (24). In addition, there is a link with increased symptom scores, as was shown in chapter five to seven (25). As recent epidemiological studies do not indicate health risks at every day levels of exposure, high risk appraisal seems inappropriate, based on current knowledge. Therefore, intervention measures targeted at informing people, to achieve a more accurate level of risk appraisal, may help to reduce the potentially negative consequences of high risk appraisal.

Despite the substantial portion of participants with high risk appraisal, the number of participants who attributed health problems to EMF was very low. In 2011/2012, only 88 (0.6%) participants attributed health problems to any EMF source, and in later years most of these participants no longer attributed health problems to EMF, showing little temporal consistency of attributions (21). Previous studies found prevalence rates of self-reported electro hypersensitivity ranging from 1,5-13.3% in different countries (26, 27). The low levels of attribution found in this study may have been an underestimation due to the way the question was worded in the questionnaires. Participants were first asked whether they currently experienced any health problem which they thought had an environmental cause, and only participants who replied to this question with "yes" received a list with potential environmental causes including EMF sources. By presenting the question this way, it is likely that only people who were very certain that EMF caused health problems showed up as attributors in the statistics. On the other hand, prevalence rates of attribution may have been overestimated in other studies through oversampling of electro hypersensitive participants, or due to the phrasing of the attribution question. Attribution rates may sometimes include participants who were uncertain about the cause of their health problems, and considered that EMF may have contributed to them when presented with this option, but who did not have prior concerns about EMF health risks. Because of the influence of the wording of questions on the prevalence rates in different studies, it is difficult to compare the results of different studies and to objectively assess the prevalence of attribution of health problems to EMF. Studies may want to carefully think about the wording of questions in their questionnaire, and reflect on the influence thereof.

It is important to distinguish between risk appraisal and attribution rates when examining the public perception of mobile phone base stations. Even when attribution rates are low, there may be widespread misconceptions about exposure levels and health risks from mobile phone base stations. High levels of risk appraisal can have consequences for public health and satisfaction of residents with their neighborhood, as well as for the acceptance of mobile phone base stations in residential areas.

Risk appraisal scores of mobile phone base stations may be in part be an expression of a more general perception toward potential environmental hazards and modern technologies, rather than a specific concern about mobile phone base stations. Studies of modern health worries previously found correlations between risk appraisal of different risks (28), and in chapter seven perceived exposure of mobile phone base stations was compared with perceived exposure of other potential environmental health hazards in the living environment. Perceived exposure of mobile phone base stations was strongly positively correlated with perceived exposure of noise and air pollution from road traffic. In part, this may be due to the clustering of environmental exposures in urban regions, and thus reflect correlations in actual exposures (29). On the other hand, more general beliefs about environmental risks, subject characteristics, and personal life experiences influence the interpretation of information about new potential health hazards (30–33). That is reflected in correlations among risk appraisal, including exposure perceptions, of different exposures in chapter seven. Risk judgment can also be driven by general beliefs about environmental risks, rather than a specific mental model including only information about base stations, and that has implications for interventions targeting risk appraisal of mobile phone base stations. It may be more difficult to influence health risk perceptions of specific potential environmental hazards such as mobile phone base stations, when these are largely an expression of a more general environmental worry.

8.3. Modelled and perceived exposure

This thesis showed that there is a very low correlation between modelled exposure and perceived exposure to RF-EMF from mobile phone base stations, indicating that most people cannot accurately estimate their own exposure. This is in line with evidence from recent experimental studies with sham exposure (34, 35), showing that people cannot report exposure levels better than chance. In observational studies, higher correlations between modelled (as a proxy of actual) and perceived exposure could be expected because participants may get clues about their exposure levels through the visibility of nearby base stations. In chapter seven we discussed that the observability of the exposure source, as well as knowledge of, or familiarity with the exposure, is likely to influence the extent to which participants are able to estimate their own exposure, and therefore the correlations between modelled and perceived exposures. It seems that the presence or absence of exposure cues has a limited impact on participants' estimations of exposure to mobile phone base stations. Other factors, such as risk perception and health concerns likely had a greater impact on perceived exposure levels.

For noise and air pollution from road traffic, which are environmental exposures with a more visible exposure source, the correlation between modelled and perceived exposure was much higher. The presence of moderate correlations between modelled and perceived (self-reported) exposures indicates that these cannot always be seen as conceptually separate predictors of health outcomes. Because the underlying causal mechanisms are not fully clear, this complicates the analysis of environmental determinants of self-reported health outcomes. In that perspective, RF-EMF from mobile phone base stations is an interesting exposure, because the low correlations with perceived exposure allow for the interpretation of modelled and perceived exposure as conceptually separate predictors in an observational cohort study. Observational studies are a valuable addition to existing experimental studies and qualitative research, as they allow for the generalization of results to real-life situations in a representative sample.

The perception of exposures can also be influenced by the presence of health problems (often described as recall bias), as well concerns about potential health risks (30). In the circumstance of an exposure-related change in the environment, these factors can have an impact on the likelihood that this environmental change is noted. Modelled RF-EMF exposure from mobile phone base stations at the home address could change over time when new antennas were added or removed, or when participants moved to a different home. For people with a substantial increase in modelled exposure in a given year, perceived exposure increased in that same year, as opposed to people with small changes or a decrease in modelled exposure. Possibly these people noted the visual change in the environment that caused the higher RF-EMF exposure. Other explanations could be that people noticed announcements in newspapers or other media, or that they heard about the change from neighbors (24). So, even though participants were generally not able to accurately estimate their own RF-EMF exposure, it appears that participants could notice changes in the environment related to changed RF-EMF exposure. Also for other exposures (noise and air pollution from road traffic) exposures changes after moving to a new home were often accompanied by corresponding changes in perceived exposures, showing that people can be aware of exposure-related changes in their environment.

8.4. Health outcomes

The results of chapter five to seven showed that not modelled, but perceived RF-EMF from mobile phone base stations was consistently associated with increased symptom scores. Because of the accurate exposure assessment and longitudinal design, this study reduced the existing uncertainty about potential health effects of RF-EMF from mobile phone base stations. Nevertheless, the results cannot exclude the possibility that there may be small effects on symptom scores in specific subgroups, or effects at much higher exposure levels, or that there are effects on other health outcomes that were not studied in this thesis. In addition, the presence of mobile phone base stations could have indirect effects on symptom scores through risk appraisal, but the importance of such mediation mechanisms depends on the underlying mechanisms. The maximum impact of such mechanisms is limited, because participants were generally not aware of the presence of base stations in the vicinity of their home. This was reflected by the low correlation between modelled and perceived exposure (r_{Sp}=0.11), but also by a low correlation between distance to the nearest antenna and perceived exposure levels (r_{Sp}=0.14). However, mediation mechanisms may play a larger role when there is an increase in exposure, as increases in modelled exposure was accompanied by increases in perceived exposure. Then, there may be long-lasting (30) effects on risk appraisal, and possibly indirectly also on symptom scores and mental health. To understand the underlying mechanisms and the temporal directionality of the relations between risk appraisal and symptom scores these were examined in chapter six.

The results of chapter six indicate that higher symptoms may precede high levels of concern about the potential health effect of exposure to RF-EMF from mobile phone base stations, as well as vice versa. Multiple mechanisms are likely to play a role simultaneously, including nocebo processes, as well as increased environmental monitoring and awareness by participants with many symptoms (30, 32, 36, 37). These findings from chapter six are valuable because they show that bidirectional associations between risk appraisal and symptom scores may exist in general population samples, even though the mean risk appraisal levels were relatively low. Nevertheless, a better understanding is needed of the relative importance of different mechanisms, as they occur in society, as this has important implications for intervention strategies. Interventions targeting high risk appraisal and negative health expectations will only be effective in reducing symptom burden if the nocebo mechanism is the main causal pathway for the association with symptom scores. In contrast, if increased environmental awareness and incorrect attribution play a large role, then interventions targeting risk appraisal are unlikely to be effective in reducing the symptom burden.

The relative importance of different mechanisms could not be determined in this study, despite the longitudinal design. In part, this was due to general population study setup. There was no specific event or intervention that could result in change in the mean population levels of modelled and perceived exposure and/or symptom scores. Also, symptoms can be temporary and recurrent, but no data was available on the duration of reported symptoms throughout the study period. The questionnaires provide snapshots of symptom experiences but there was no data on the intermittent periods. Intermittent periods of both symptom experiences and high risk appraisal may have occurred unnoticed between the timing of different questionnaires. Future studies may improve by increasing the number of measurements. A large number of measurements with short time intervals may allow for easier identification of temporal relations between the different variables. Even then, observational studies have their limitations, because important factors cannot be controlled, contrary to experimental research. However, results from experimental research cannot easily be translated to society, and the number of factors that can be studied simultaneously is limited. To understand the role of important political and cultural factors, a sociological approach may be better suited. In summary, a combination of different research approaches is needed. Communication between different research disciplines may contribute to achieving a better understanding of the different processes that play a role.

One of the main health outcomes in this thesis was the overall score on the 4DSQ-s symptom questionnaire. In order to interpret the results of this study, it is important to understand what this symptom score means. In psychology, a high symptom score on this type of questionnaires is often interpreted as a possible indication of a somatoform disorder. In the past, a distinction was made between patients with symptoms with a known medical explanation, and patients with symptoms without a known medical explanation, for which a psychogenic cause could be assumed. This distinction was hard to make in practice, and studies (38–40) have shown that somatic symptoms have a substantial impact on daily functioning and health care use, regardless of the presence or absence of a known medical explanation for these symptoms. In many cases, both biological and psychosocial factors will play a role in symptom experiences (41, 42). In this thesis, the focus is on health effects on the overall symptom score, a combination of both number of symptoms and intensity of these symptoms. The overall symptom score does not provide specific information about which specific symptoms, or patterns of symptoms are associated with perceived exposure to mobile phone base stations. An association between environmental exposure and groups of symptoms, but not all symptoms, is common when there are biological mechanisms that specifically cause that type of symptoms. However, also when perceived exposure is responsible for increased symptoms it is possible to find associations with some, but not all symptoms. Psychosocial factors, such as knowledge and expectations about the exposure can influence the type of symptoms that people report (23, 43). Chapter 5 also includes results of analyses with individual symptoms as outcome variables. Not only was perceived exposure associated with a higher overall symptom score, but also with nearly all measured individual symptoms such as headache, dizziness, chest pain, and back pain. A disadvantage of these analyses, using either the total symptom score, or the presence or absence of individual symptoms, is that it ignores the underlying structure of the symptom questionnaire. An analysis of the total symptom score cannot provide insight into whether only some individual symptoms, or specific groups of symptoms, such as musculoskeletal symptoms are affected. Analyses of all individual symptoms separately ignores the dependencies among different symptoms, with an increased chance of false discoveries. Chapter four examined the factor structure underlying the 4-DSQ-s symptom questionnaire (44). A bi-factor structure fit the data well. This model assumes that scores on the questionnaire items are in part due to general factor. i.e. representing a general tendency to report symptoms, and in part due to a number of specific factors. Ideally the underlying factor structure of the questionnaire would be taken into account when analyzing effects of perceived and modelled exposure to achieve a better insight into the specificity of effects on self-reported symptoms. This calls for the development of new analytical techniques that can easily be used in applied research.

8.5. Implications for future research

There have been many studies into the potential health effects of RF-EMF exposure, and so far, there seems little reason for concern. This raises the question of whether more similar follow-up research is an efficient use of the available resources. Some uncertainty about health effects remains due to inaccuracies in exposure assessment and the difficulty of studying health effects that may occur only in sensitive subgroups of the population. As long as there is no known biological mechanism pointing to specific health effects, continued epidemiological research may be inefficient to identify small effects, or effects in small subgroups. However, research in this area must be prepared for rapid technological and societal changes in the field of mobile technology, that may alter the potentiality for health effects. In addition, there is the possibility of indirect effects of RF-EMF exposure sources on symptom scores through risk appraisal, in particular when people experience involuntary changes that affect perceived and/or actual exposure in their residential environment. The occurrence of such indirect effects may also be effected by technological changes. The design of the network architecture for mobile networks in residential areas, as well as the local procedures for required permits, may influence the levels of risk appraisal. With the upcoming introduction of new mobile 5G networks, and the phasing out of older networks, levels of risk appraisal in the general population and indirect effects on symptom scores could change. There is a trend toward the use of micro stations and femtocells, which are less likely to be noticed by residents, but greater in number.

There are also ethical arguments for continued research into health effects of RF-EMF. A substantial portion of the population is still concerned about the potential health effects of RF-EMF. The availability of accurate and up-to-date information through continued research, may contribute to sustaining trust of the general population in the responsible authorities. At the same time, presenting the research findings in the media itself can increase the health concerns in the population (23), which is an undesirable effect if these health concerns are unnecessary, especially if these concerns may increase symptom burden.

An extension of the analytical approach for RF-EMF exposure to other environmental exposures and symptom scores showed similar results regarding the role of exposure perceptions, with important implications for epidemiological and psychosocial research into environmental determinants of self-reported health outcomes. Chapter seven in this thesis examined three environmental exposures (RF-EMF from mobile phone base stations, noise from road traffic, and air pollution from road traffic). In contrast to RF-EMF, modelled noise and air pollutants were generally associated with increased symptom scores, regardless of the type of symptoms that were assessed. Similarly, perceived exposure was consistently associated with increased symptom scores. High perceived environmental exposures were also correlated with their corresponding modelled exposures, especially in the case of noise and air pollution from road traffic. When both modelled and perceived exposure were analyzed as predictors in a single model, the effect of modelled exposure generally disappeared or severely diminished. Prior epidemiological studies may have incorrectly ascribed significant effects of actual exposure on symptom scores by ignoring the role of risk appraisal. However, it is uncertain to what extent this kind of bias occurs, especially because much is unknown about the relative importance of the underlying causal psychosocial mechanisms. Here lies an important role for psychosocial research.

8.6. Recommendations for society

This thesis did not find any direct effects of RF-EMF exposure levels in the residential environment on symptom based health outcomes. Based on these findings is unnecessary to take efforts to reduce RF-EMF exposure from mobile phone base stations. This thesis focused on symptom based health outcomes only, and can therefore not exclude the possibility that there may be other health effects, or health effects in sensitive subgroups of the population. However, the availability of scientific evidence from other reliable sources currently gives no reason for concern regarding health effects of actual exposure to RF-EMF from mobile phone base stations.

A substantial portion of the AMIGO cohort indicated that they think exposure to RF-EMF is high and are concerned about its potential health effects. These people are at risk of increased symptom scores (25, 45). There can be many factors influencing symptom reporting (39, 42), and often the causes of an individuals' symptom experiences are unknown. Because everyone occasionally experiences some of these symptoms, such as headache or back pain, higher symptom scores may not appear like a large health issue. However, regardless of whether the causes are known, people who experience more symptoms report a lower quality of life and more health care use, and therefore preventive measures are needed (38, 40, 42). Citizens who search for health information about RF-EMF often find alarming and inaccurate information on the internet. It is important to improve the public access to accurate and accessible information to prevent unnecessary concerns. In specific situations which may provoke public resistance, such as the placement of new base stations, it could help to actively communicate with the public about health information. Previous research (46) found that people often feel that the information they receive is not tailored to their needs, for example because it was overly focused on technical information or procedures, rather than address their concerns about health effects or effects on property values. At the same time, actively providing information about health risks can sometimes inadvertently increase health concerns especially when trust in the responsible authorities is low (23, 47). Therefore, a balance should be found between actively and passively providing health information about RF-EMF exposure.

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English summary

Technological changes have led to a rapid increase in the use of mobile technology. This is coupled with an increase in the number of mobile phone base stations that emit radiofrequency electromagnetic fields (RF-EMF). There are concerns about the potential health effects of this exposure among experts and citizens. Some people attribute symptoms such as headaches and dizziness to RF-EMF exposure. Up until now, scientific studies have not shown convincing evidence of adverse health effects associated with RF-EMF exposure in the everyday environment. Psychosocial mechanisms can also play a role in symptom experiences, but the exact role of such mechanisms in the general population in combination with the role of actual exposure is not clear. Uncertainty about the potential health effects remains, in part due to the unavailability of accurate exposure assessment methods that are feasible for use in epidemiological research. The aim of this study was to assess the role of both modelled (an objective estimate of actual) and perceived exposure to RF-EMF from mobile phone base stations in non-specific symptom reporting. The study applied a longitudinal study design that combined insights from recent epidemiological and psychosocial studies.

To achieve this aim, we first examined the applicability of a geospatial model (NISMap) for use in epidemiological research. We assessed whether an estimation of RF-EMF exposure from mobile phone base stations at the home address, corresponds with personal exposure levels. We compared model predictions at the home address with personal 24h and 48h measurements in two separate measurement studies. Chapter two and three showed that this model can be used to meaningfully rank individuals on exposure levels (correlation between 48h measurements and model predictions: r_{Sp}=0.47). The model was more accurate than previously used methods such as estimating the distance between the nearest antenna and the home. Nevertheless, there was considerable exposure misclassification, reducing the power to detect health effects and implying a need for large sample sizes in epidemiological studies. The application of geospatial models instead of alternative methods such as area measurements with interpolation, or personal measurements has advantages. Obtaining the required data does not require labour-intensive measurements, and an increase in the number of participants or the size of the modeled geographical area does not come with a linear increase in the cost of data collection, unlike personal measurements. These advantages make geospatial models such as NISMap attractive for use in epidemiological research.

In the second part of this thesis, data was analyzed from the Dutch AMIGO cohort. Exposure to RF-EMF from mobile phone base stations was modeled at the home address of AMIGO participants using the geospatial model NISMap. Over time, the model estimations were updated with new data regarding the locations and characteristics of antennas, and with updated information about the home address of participants. Questionnaires were sent out in 2011/2012, 2013, 2014, and 2015 to obtain repeated information on perceived exposure, risk perception, health concerns, and symptom experiences.

AMIGO participants were asked to what extent they thought they were exposed to RF-EMF from mobile phone base stations. A majority (approximately 75%) of our respondents choose a score of 0 or 1 on a scale of 0-6, which indicates that most participants thought their exposure to RF-EMF was low. A sizable minority (approximately 25%) reported higher levels of perceived exposure. Participants were also asked whether they thought that this exposure could be a health risk, and if they were concerned about their personal health because of RF-EMF exposure from mobile phones. Most participants did not indicate that RF-EMF exposure was a great health risk, and most were not highly concerned about the potential health risks of RF-EMF exposure. People who thought they were exposed to RF-EMF from mobile phone base stations more often thought that this exposure could be a health risk, and were also more likely to be concerned about the potential health risks of this exposure. These three perceptions were grouped under the term risk appraisal in this thesis. Differences between elements of risk appraisal and their role in individual health responses to mobile phone base stations were discussed in chapter six. Mean levels of risk appraisal varied across subjects with different subject characteristics. Women, participants with a high education, and participants with high trait negative affect (a tendency to experience negative emotions) reported higher levels of risk appraisal.

To evaluate the extent to which participants can accurately estimate their own exposure the questionnaire information on perceived exposure was compared with the model estimates. There was a weak correlation between modelled and perceived exposure ($r_{Spearman}$=0.10). Probably, the fact that exposure cannot be sensed directly contributed to the low correlation. In addition, the exposure sources; antenna's, are not always visible from the home. Furthermore, the lack of public knowledge about RF-EMF exposure from mobile phone base stations likely contributed to the low correlation. Finally, exposure misclassification may explain the low correlation with perceived exposure to some extent. Chapter seven also compares correlations between modelled and perceived exposures for other environmental exposures, namely noise ($r_{Spearman}$=0.40) and air pollution ($r_{Spearman}$=0.34) from road traffic. Here, much higher correlations between modelled exposure and their corresponding perceived exposures were observed, in particular for noise. In the case of noise from road traffic, this exposure can be directly perceived by the auditory system. Also, the exposure source itself, road traffic in the residential environment, is easily identified. For air pollution from road traffic, the exposure source is the same as for noise, but the exposure itself cannot be directly perceived. Sometimes smell can be an indication of air pollution, but smell is not an accurate proxy of exposure to particulate matter from road traffic. In summary, depending on the observability of the exposure, or the exposure source, there is variation in the extent to which participants can estimate their exposure levels. It was possible to also analyze the impact of a change in exposure, for participants who moved to a different home, or because of updated model estimations over time. In the case of changes in modelled exposures the data indicated that these changes are often accompanied by corresponding changes in perceived exposures, showing that people can be aware of exposure-related changes in their environment.

Chapter five evaluates the impact of both modelled and perceived exposure to RF-EMF from mobile phone base stations on self-reported health outcomes. Modelled RF-EMF exposure from mobile phone base stations was not associated with self-reported symptoms. If such health effects exist at every day levels of exposure, they are likely to be small, or to occur (only) in sensitive subgroups of the population (that have not yet been identified). In contrast, higher risk appraisal of mobile phone base stations was consistently associated with reporting higher symptom scores in chapter five and six. The temporal directionality of the effects was examined in chapter six. There was some evidence of bidirectional temporal associations between risk appraisal and symptom scores. The results of chapter six indicate that higher symptom scores may temporally precede higher levels of concern about the potential health effect of exposure to RF-EMF from mobile phone base stations, as well as vice versa. No such temporal associations were found for other indicators of risk appraisal. This finding implies that multiple mechanisms are likely to play a role simultaneously, including nocebo processes (nocebo: the expectation that negative health effects may occur can have an adverse impact on symptom experiences). In addition, mechanisms in the opposite causal direction can play a role. For example, participants with many symptoms may monitor their environment more actively (increased environmental monitoring), and become more aware of suspected potential causes of their symptoms. These participants may report and recall exposures differently than healthy participants, also described as recall bias in epidemiological research.

For noise and air pollution from road traffic, modelled exposures were associated with increased symptom scores, as was shown in chapter seven. However, perceived exposures showed overall stronger associations with symptom scores than modelled exposures. For perceived, and generally also for modelled exposures, associations with symptom scores were not specific to individual symptoms or symptom scores. Effects were relatively greater for non-specific symptom scores than for more specific outcomes (sleep disturbance and respiratory symptoms). The lack of specificity of health effects means it is difficult to disentangle health effects of modelled and perceived exposures. When biological mechanisms are responsible for health effects, it seems more likely that health effects would be specific for individual symptoms or groups of symptoms, rather than general effects on all measured symptoms. However, specific health effects are also possible when perceived exposure is responsible for increased symptom scores, for example when specific negative health expectations arise after media reports. In the case of RF-EMF, the potential biological mechanisms are unknown, and it is uncertain what kind of health effects can be expected. The general approach in epidemiological analyses is then to either analyze effects on an overall symptom score, or on individual symptoms. Neither of these approaches are ideal, as was discussed in chapter four, because they do not take into account that multiple factors that play a role in symptom reporting. Chapter four analyzed the factor structure of the 4-DSQ-s symptom questionnaire and showed that a bi-factor structure fitted the data well. In this model, there is a general factor underlying symptom scores, as well as specific factors. Ideally, statistical analyses would separate effects of predictors on general symptom reporting from effects on specific symptom reporting, but in practice this is difficult.

When both modelled and its corresponding perceived exposure were included as predictors in a single model, the impact of modelled exposures on symptom scores disappeared or strongly diminished. The interpretation of these findings depends on the relative importance of the mechanisms underlying the associations between risk appraisal and symptom scores. In part, for participants with high risk appraisal the expectation that negative health effects may occur can have an adverse effect on symptom experiences (nocebo) when participants think they are exposed. Because of the apparent influence of actual exposure sources (and therefore exposure, with modelled exposure as a proxy) on perceived exposure, especially in the case of changes in exposure, it seems that there may be indirect effects of exposure on symptom scores. The direct health effects of exposures may then be biased in epidemiological studies when risk appraisal is not taken into account. On the other hand, if processes such as increased environmental monitoring are mainly responsible for associations between risk appraisal symptom scores, the implications for interpretation, policy, and effective interventions are different, as was discussed in chapter eight.

Conclusion

The results did not show evidence of adverse effects of exposure to RF-EMF from mobile phone base stations on symptom reporting. Risk appraisal does play an important role in symptom reporting, but the etiological role is not fully clear. Risk appraisal appears to be influenced by exposure cues in the residential environment, and the presence of these exposure cues may have indirect effects on health through an increase in risk appraisal. This thesis raises a series of important questions for epidemiological and psychosocial research disciplines, with potential major implications for interpretation of research findings and policy. Further integration of different research disciplines may in the future contribute to reaching new insights into the relative importance of different causal mechanisms.

Nederlandse samenvatting

Technologische veranderingen hebben geleid tot een snelle toename in het gebruik van mobiele telefoons. Dat gaat gepaard met een toename in het aantal zendmasten voor mobiele telefonie. Deze zendmasten zenden radiofrequente elektromagnetische velden (RF-EMF) uit, waaraan de omgeving wordt blootgesteld. Zowel onder experts als in de algemene populatie bestaan er zorgen over de mogelijke gezondheidseffecten van deze blootstelling.
Sommige mensen hebben gezondheidsklachten zoals hoofdpijn en duizeligheid die zij toeschrijven aan RF-EMF blootstelling. Tot nu toe is er geen overtuigend wetenschappelijk bewijs van negatieve gezondheidseffecten door RF-EMF blootstelling in de dagelijkse leefomgeving. Psychosociale mechanismen kunnen ook een rol spelen in het ervaren van gezondheidsklachten, maar de precieze rol van zulke mechanismen in de algemene populatie, in combinatie met de rol van werkelijke blootstelling is niet duidelijk. Tot nu toe is er nog steeds onduidelijkheid over de mogelijke gezondheidseffecten. Ten dele komt dat door het ontbreken van nauwkeurige methoden om de blootstelling te bepalen, die geschikt zijn voor gebruik in epidemiologisch onderzoek. Het doel van deze studie was om de rol van gemodelleerde (een objectieve schatting van de werkelijke) en ervaren blootstelling aan RF-EMF van zendmasten voor mobiele telefonie te onderzoeken in relatie tot het rapporteren van aspecifieke gezondheidsklachten. Daarvoor is een longitudinale onderzoeksopzet toegepast, waarbij inzichten uit recent epidemiologisch en psychosociaal onderzoek werden toegepast en gecombineerd.

In het eerste deel van dit project hebben we onderzocht of een georuimtelijk model (NISMap) geschikt is voor gebruik in epidemiologisch onderzoek. We hebben geanalyseerd of een schatting van blootstelling gebaseerd op het huisadres goed overeenstemde met het persoonlijke blootstellingsniveau. Daarvoor hebben we twee aparte studies gedaan, waarin de modelschattingen op het huisadres werden vergeleken met persoonlijke metingen (meetperiodes van 24 uur/48 uur). Hoofdstuk twee en drie hebben aangetoond dat NISMap in staat is om individuen betekenisvol te rangschikken naar blootstellingsniveau (de Spearman correlatie tussen 48 uurs metingen en modelschattingen was 0.47). Deze methode is nauwkeuriger dan eerder toegepaste methoden zoals het schatten van de afstand tussen de dichtstbijzijnde antenne en het huis. Echter, er is wel sprake van substantiële misclassificatie. Dit zorgt dat epidemiologische studies minder kans hebben om een bestaand gezondheidseffect te vinden, en daarom zijn er grote aantallen studiedeelnemers nodig. Er zijn voordelen aan het gebruik van georuimtelijke modellen ten opzichte van alternatieve methoden zoals het gebruik van persoonlijke metingen, of de interpolatie van gemeten blootstelling op verschillende punten. Er is namelijk minder personeel nodig dat veel tijd moet besteden aan het uitvoeren van de metingen. Ook nemen de kosten van dataverzameling niet lineair toe naarmate er meer deelnemers zijn, of de deelnemers verspreid zijn over een groter geografisch gebied. Dankzij deze voordelen is het aantrekkelijk om georuimtelijke modellen zoals NISMap te gebruiken in epidemiologisch onderzoek.

In het tweede deel van deze scriptie is data geanalyseerd van het Nederlandse AMIGO (Arbeid, Milieu, en Gezondheid Onderzoek) cohort. De blootstelling aan RF-EMF van zendmasten voor mobiele telefonie werd gemodelleerd met het georuimtelijke model NISMap. Gedurende de tijd zijn de modelschattingen geüpdatet met nieuwe informatie over de locaties en kenmerken van antennes, en met nieuwe informatie over het huisadres van de deelnemers. De deelnemers hebben ook uitnodigingen ontvangen om deel te nemen aan vragenlijsten, in 2011/2012, 2013, 2014, en 2015. Zo konden we herhaalde informatie vergaren over ervaren blootstelling, risicoperceptie, zorgen over gezondheidseffecten, en ervaren gezondheidsklachten.

Aan de AMIGO deelnemers is gevraagd in welke mate zij denken te worden blootgesteld aan RF-EMF. Een meerderheid (ca 75%) van de deelnemers koos een waarde van 0 of 1 op een schaal van 0 tot 6. Dit geeft aan dat de meeste deelnemers dachten dat hun blootstelling laag was. Er was wel een grote minderheid (ca 25%) die hogere niveaus van ervaren blootstelling rapporteerden. Er werd ook aan de deelnemers gevraagd of ze dachten dat blootstelling een gezondheidsrisico kon zijn, en of zij zich zorgen maakten over de mogelijke gevolgen van blootstelling voor hun eigen gezondheid. De meeste deelnemers dachten niet dat RF-EMF een groot risico vormt voor de gezondheid, en waren ook niet bezorgd over de mogelijke gevolgen voor hun eigen gezondheid. Mensen die rapporteerden dat hun blootstelling hoog was, dachten ook vaker dat blootstelling een gezondheidsrisico was, en maakten zich meer zorgen over de gevolgen voor hun eigen gezondheid. Deze drie gerapporteerde percepties zijn gegroepeerd onder de term risicobeleving. Verschillen tussen deze elementen van risicobeleving en in hun rol in het rapporteren van gezondheidsklachten zijn besproken in hoofdstuk zes. De gemiddeld gerapporteerde niveaus van risicobeleving varieerde tussen deelnemers met verschillende persoonskenmerken. Vrouwen, deelnemers met een hogere opleiding, en deelnemers die over het algemeen veel negatieve emoties ervaren rapporteerden hogere niveaus van risicobeleving.

Om te evalueren in welke mate deelnemers in staat zijn om zelf hun blootstellingsniveau in te schatten hebben we de vragenlijst informatie over ervaren blootstelling vergeleken met de modelschattingen. Er was een zwakke samenhang tussen gemodelleerde en gemeten blootstelling ($r_{Spearman}$=0.10). Wat waarschijnlijk heeft bijgedragen aan de zwakke samenhang is het feit dat het niet mogelijk is om blootstelling direct zintuiglijk waar te nemen. Daarnaast zijn de blootstellingsbronnen (zendmasten) niet altijd goed zichtbaar in de woonomgeving. Ook kan een gebrek aan kennis (over RF-EMF blootstelling) in de samenleving een rol spelen bij de zwakke samenhang tussen gemodelleerde en ervaren blootstelling. Ten slotte is het mogelijk dat misclassificatie van gemodelleerde blootstelling een rol speelde. In hoofdstuk zeven is ook voor andere omgevingsblootstellingen de samenhang tussen gemodelleerde en ervaren blootstelling onderzocht, namelijk voor geluid ($r_{Spearman}$=0.40) en luchtvervuiling ($r_{Spearman}$=0.34) van wegverkeer in de woonomgeving. De samenhang tussen gemodelleerde en ervaren blootstelling was hier veel sterker. In het geval van geluid zal het een rol spelen dat het mogelijk is om deze blootstelling direct zintuiglijk waar te nemen (te horen). Ook is het eenvoudig mogelijk om te bron van de blootstelling (wegverkeer) te identificeren. De bron van de blootstelling was gelijk voor luchtvervuiling, maar de blootstelling zelf kan minder makkelijk worden waargenomen, hoewel geur soms een indicatie kan geven dat men is blootgesteld aan luchtvervuiling. Kortom, afhankelijk van de mate waarin de blootstelling, of de bron, kan worden waargenomen, is er variatie in de mate waarin deelnemers hun blootstelling kunnen inschatten. Voor een deel van de deelnemers was het mogelijk om te onderzoeken in welke mate verandering in de gemodelleerde blootstelling invloed had op de ervaren blootstelling. De resultaten laten zien dat verandering in gemodelleerde blootstelling vaak gepaard gaat met corresponderende veranderingen in ervaren bloostelling. Dit toont aan dat mensen zich bewust kunnen zijn van blootstelling gerelateerde veranderingen in hun omgeving.

In hoofdstuk vijf wordt de impact van zowel gemodelleerde als ervaren blootstelling aan RF-EMF van zendmasten op het rapporteren van gezondheidsklachten onderzocht. Gemodelleerde RF-EMF blootstelling hing niet samen met zelf-gerapporteerde gezondheidsklachten. Als zulke gezondheidseffecten bestaan, dan zijn ze waarschijnlijk klein, of treden ze alleen op in bepaalde gevoelige groepen in de samenleving (zulke groepen zijn tot nu toe niet geïdentificeerd). In tegenstelling tot gemodelleerde blootstelling waren ervaren blootstelling en risicobeleving consistent geassocieerd met het rapporteren van hogere klachtenscores in hoofdstuk vijf en zes. In hoofdstuk zes is ook de richting van deze verbanden over de tijd onderzocht. We hebben enig bewijs gevonden van het bestaan van verbanden tussen risicobeleving en klachtenscores over de tijd in beide richtingen. Hogere klachtenscores gingen vooraf aan het rapporteren van meer zorgen over de eigen gezondheid, maar ook het omgekeerde verband werd gevonden. Voor de andere elementen van risicobeleving zijn niet zulke effecten over de tijd gevonden. Het is waarschijnlijk dat diverse psychosociale mechanismen een rol spelen bij het verband tussen risicobeleving en klachten. Zo spelen nocebo processen mogelijk een rol, wat inhoudt dat de verwachting dat negatieve gezondheidseffecten zouden kunnen optreden een ongunstige impact heeft op gezondheidsklachten.

Daarnaast kunnen mechanismen in de tegenovergestelde causale richting een rol spelen. Deelnemers met veel gezondheidsklachten zijn mogelijk meer bezig met het actief volgen van hun omgeving, en worden ze zich dan meer bewust van mogelijke omgevingsoorzaken van hun gezondheidsklachten. Deelnemers met veel gezondheidsklachten kunnen blootstelling anders ervaren en rapporteren dan gezonde deelnemers, wat ook omschreven wordt als recall bias in epidemiologisch onderzoek.

In tegenstelling tot gemodelleerde RF-EMF was er sprake van samenhang tussen gemodelleerde blootstelling aan geluid en luchtvervuiling door wegverkeer, en een toename aan gezondheidsklachten, zoals aangetoond in hoofdstuk zeven. Echter, de samenhang tussen ervaren blootstellingen en gezondheidsklachten was sterker voor alle onderzochte omgevingsblootstellingen (RF-EMF, geluid, en luchtvervuiling). Als we kijken naar het soort klachten dat samenhing met ervaren en gemodelleerde blootstellingen, was daarin geen duidelijk patroon van individuele of groepen klachten te ontdekken. Gezondheidseffecten leken sterker voor aspecifieke klachten (een uitkomstmaat bestaande uit allerlei gezondheidsklachten) dan voor meer specifieke uitkomstmaten (slaapproblemen en respiratoire symptomen). Omdat de gevonden gezondheidseffecten aspecifiek zijn is het lastig om deze te ontwarren, en toe te schrijven aan specifieke gemodelleerde of ervaren blootstellingen. Als biologische mechanismen verantwoordelijk zijn voor gezondheidseffecten, is het aannemelijk dat er specifieke gezondheidseffecten optreden, in plaats van slechts aspecifieke effecten. Specifieke gezondheidseffecten zijn echter ook mogelijk als ervaren blootstelling verantwoordelijk is voor een toename in gezondheidsklachten, bijvoorbeeld als er specifieke negatieve verwachtingen optreden na berichten in de media. De potentiele biologische mechanismen zijn onbekend in het geval van RF-EMF, en het is onzeker wat voor soort gezondheidseffecten zouden kunnen optreden. In zo'n geval is de typische aanpak in epidemiologisch onderzoek om een uitkomstmaat te gebruiken bestaande uit een totaalscore van gezondheidsklachten, ofwel om effecten op individuele klachten te analyseren. Beide benaderingen hebben nadelen, zoals besproken in hoofdstuk vier, omdat er geen rekening wordt gehouden met de vele factoren die een rol kunnen spelen bij het rapporteren van klachten. Hoofdstuk vier analyseert de factor structuur van de 4-DSQ-s vragenlijst voor gezondheidsklachten, en laat zien dat een bi-factor structuur met zowel een algemene factor als een aantal specifieke factoren goed bij de data past. Idealiter zouden statistische analyses effecten van determinanten op het rapporteren van klachten in het algemeen scheiden van effecten op specifieke factoren, maar in de praktijk blijkt dit lastig te zijn.

De associaties tussen gemodelleerde blootstellingen en het rapporteren van gezondheidsklachten verdwenen meestal wanneer de bijbehorende ervaren blootstelling ook werd meegenomen in het model. Alleen het effect van de ervaren blootstelling op gezondheidsklachten was dan significant. De interpretatie van deze bevinding is afhankelijk van het relatieve belang van de verschillende mogelijke verklaringen voor de relatie tussen risicobeleving en gezondheidsklachten. Ten dele kan het nocebo mechanisme een rol spelen als men denkt te worden blootgesteld, en verwacht dat deze blootstelling mogelijk ongunstige gezondheidseffecten kan hebben. Omdat de aanwezigheid van blootstellingsbronnen (en dus blootstelling) invloed lijkt te hebben op ervaren blootstelling, in het bijzonder wanneer er sprake is van veranderingen in blootstelling, kan het zijn dat de aanwezigheid van blootstellingsbronnen indirect invloed heeft op gezondheidsklachten. De directe effecten van blootstelling kunnen dan verkeerd worden ingeschat in epidemiologisch onderzoek, als er geen rekening wordt gehouden met de rol van risicobeleving van de deelnemers. Daarentegen, als omgekeerde causale mechanismen juist een belangrijke rol spelen, heeft dat andere implicaties voor de interpretatie, beleid, en effectieve interventies, zoals beargumenteerd in hoofdstuk acht.

Conclusie

De resultaten tonen geen bewijs van negatieve effecten van blootstelling aan RF-EMF van zendmasten op gezondheidsklachten. Risicobeleving speelt wel een belangrijke rol bij het rapporteren van gezondheidsklachten, maar de etiologische rol is nog niet volledig duidelijk. Risicobeleving lijkt te worden beïnvloed door de aanwezigheid van blootstellingsindicatoren in de leefomgeving, en deze blootstellingsindicatoren kunnen zo indirect effect hebben op de gezondheid via toegenomen risicobeleving. Dit onderzoek werpt een aantal belangrijke vragen op voor zowel epidemiologisch als psychosociaal onderzoek, met mogelijk grote implicaties voor de interpretatie van onderzoeksbevindingen en beleid. In de toekomst kan verdere integratie van verschillende onderzoek disciplines mogelijk bijdragen aan het bereiken van nieuwe inzichten in het relatieve belang van de verschillende causale mechanismen die een rol spelen bij het rapporteren van (mogelijk) omgeving gerelateerde gezondheidsklachten.

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Curriculum Vitae

Astrid Martens was born on October 27th in 1988 in Albrandswaard, the Netherlands. She completed secondary school at Blaise Pascal in Spijkenisse in 2007, with her study program focused on subjects in nature and health (natuur en gezondheid). During high school, Astrid became interested in scientific research after being inspired and guided by her biology teachers Carin Cornelissen and Boris Börger. She then proceeded to study psychology at the Universiteit Leiden, and received her Bachelor's degree in 2010. Astrid further developed her special interest in doing research during her university years, and decided to move forward with a master program that would improve her knowledge of research methodology. She did her internship at the Erasmus Medical Center in Rotterdam where she investigated the effect of chronic pain in adolescents on their quality of life. Astrid completed her master Methodology and Statistics in Psychology in 2012 at the Universiteit Leiden. The title of her master thesis was "The ideal point classification model with random effects". After she graduated, she started her PhD project, leading to this thesis at the Universiteit Utrecht, in collaboration with the VUMC (Amsterdam). During her PhD, Astrid followed several courses to broaden and strengthen her knowledge in epidemiology and environmental health. The main findings of this thesis, the effects of modeled and perceived exposure of RF-EMF from mobile phone base stations on non-specific symptoms, were presented at the international European Public Health conference in Vienna, in November 2016.

List of Publications

Martens, A. L., Bolte, J. F. B., Beekhuizen, J., Kromhout, H., Smid, T., & Vermeulen, R. C. H. (2015). Validity of at home model predictions as a proxy for personal exposure to radiofrequency electromagnetic fields from mobile phone base stations. Environmental Research, 142, 221–226. https://doi.org/10.1016/j.envres.2015.06.029

Martens, A. L., Slottje, P., Meima, M. Y., Beekhuizen, J., Timmermans, D., Kromhout, H., … Vermeulen, R. C. H. H. (2016). Residential exposure to RF-EMF from mobile phone base stations: Model predictions versus personal and home measurements. Science of The Total Environment, 550, 987–993. https://doi.org/10.1016/j.scitotenv.2016.01.194

Martens, A. L., Slottje, P., Timmermans, D. R. M., Kromhout, H., Reedijk, M., Vermeulen, R. C. H., & Smid, T. (2017). Modeled and Perceived Exposure to Radio-Frequency Electromagnetic Fields From Mobile-Phone Base Stations and the Development of Symptoms Over Time in a General Population Cohort. American Journal of Epidemiology, 1–10. https://doi.org/10.1093/aje/kwx041

Martens, A. L., Porsius, J. T., Slottje, P., Claassen, L., Korevaar, J. C., Timmermans, D. R. M., … Smid, T. (2015). Somatic symptom reports in the general population: Application of a bi-factor model to the analysis of change. Journal of Psychosomatic Research, 79(5), 378–383. https://doi.org/10.1016/j.jpsychores.2015.09.006

Martens, A. L., Slottje, P., Timmermans, D. R. M., Kromhout, H., Reedijk, M., Smid, T., Vermeulen, R. C. H. (2017). Reply to letter to the editor by Dr. Mortazavi on our article "Modeled and Perceived Exposure to Radio-Frequency Electromagnetic Fields from Mobile-Phone Base Stations and the Development of Symptoms Over Time in a General Population Cohort". American Journal of Epidemiology.

Martens, A. L., Reedijk, M., Smid, T., Huss, A., Timmermans, D.R.M., Strak, M., Houthuijs, D., Lenters, V., Kromhout, H., Verheij, R., Slottje, P., Vermeulen, R.C.H. Modeled and perceived RF-EMF, noise and air pollution and symptoms in a population cohort. Is perception key in predicting symptoms? Submitted for publication

Martens, A. L., Slottje, P., Smid, T., Kromhout, H., Vermeulen, R.C.H, Timmermans, D.R.M. Longitudinal associations between risk appraisal of base stations and non-specific symptoms. Submitted for publication

Presentations

Martens, A. L., Slottje, P., Timmermans, D.R.M., Kromhout, H., Yzermans, C.J, Korevaar, J.C., Vermeulen, R.C.H., Smid, T. Mobile phone base stations and health complaints, a longitudinal analysis comparing perceived and actual exposure (june 2013) annual meeting of the Netherlands epidemiological society (Weon), Utrecht, the Netherlands (moderated poster presentation).

Martens, A. L., Slottje, P., Timmermans, D.R.M., Kromhout, C.J, Korevaar, J.C., Smid, T., Vermeulen, R.C.H. (nov 2015) Perceived and modelled exposure to RF-EMF from mobile phone base stations and the development of non-specific symptoms International Society for Environmental Epidemiology (ISEE), Utrecht, the Netherlands (oral presentation).

Martens, A. L., Slottje, P., Timmermans, D.R.M., Kromhout, H., Vermeulen, R.C.H, Smid, T. (nov 2016) Actual and perceived exposure to base stations and non-specific symptoms in a longitudinal study. Amsterdam Public Health Annual Meeting Amsterdam, the Netherlands (poster presentation).

Martens, A. L., Slottje, P., Timmermans, D.R.M., Kromhout, H., Vermeulen, R.C.H, Smid, T. (nov 2016) Actual and perceived exposure to base stations and non-specific symptoms in a longitudinal study. The European Journal of Public Health, 26, ckw171 (oral presentation).