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Clinically defined non-specific symptoms in the vicinity of mobile phone base stations: A retrospective before-after study

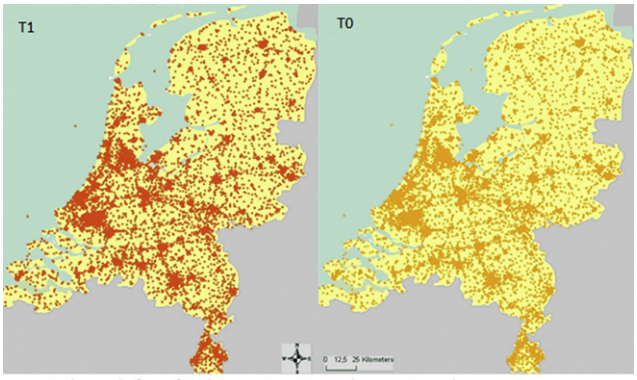
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HIGHLIGHTS

- There was an important increase in the total number of MPBS at T1 compared to T0.
- Prevalence of NSS was generally higher at T1 especially in the MPBS-sensitive group.
- Exposure from MPBS was not associated with NSS in the total sample.
- Some interactions were observed between exposure and MPBS-sensitivity on NSS risk.
- Studies of longitudinal design are needed, focusing on susceptible subgroups.

GRAPHICAL ABSTRACT



Applying a before-after design to investigate the association between exposure to mobile phone base stations and non-specific symptoms

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ABSTRACT

The number of mobile phone base station(s) (MPBS) has been increasing to meet the rapid technological changes and growing needs for mobile communication. The primary objective of the present study was to test possible changes in prevalence and number of NSS in relation to MPBS exposure before and after increase of installed MPBS antennas. A retrospective cohort study was conducted, comparing two time periods with high contrast in terms of number of installed MPBS. Symptom data were based on electronic health records from 1069 adult participants, registered in 9 general practices in different regions in the Netherlands. All participants were living within 500 m from the nearest bases station. Among them, 55 participants reported to be sensitive to MPBS at T1. A propagation model combined with a questionnaire was used to assess indoor exposure to RF-EMF from MPBS at T1. Estimation of exposure at T0 was based on number of antennas at T0 relative to T1.
At T1, there was a >30% increase in the total number of MPBS antennas. A higher prevalence for most NSS was observed in the MPBS-sensitive group at T1 compared to baseline. Exposure estimates were not associated with GP-registered NSS in the total sample. Some significant interactions were observed between MPBS-sensitivity and

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exposure estimates on risk of symptoms. Using clinically defined outcomes and a time difference of >6 years it was demonstrated that RF-EMF exposure to MPBS was not associated with the development of NSS. Nonetheless, there was some indication for a higher risk of NSS for the MPBS-sensitive group, mainly in relation to exposure to UMTS, but this should be interpreted with caution. Results have to be verified by future longitudinal studies with a particular focus on potentially susceptible population subgroups of large sample size and integrated exposure assessment.
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1. Introduction

The association between everyday life exposure to radiofrequency electromagnetic fields (RF-EMF) and various health complaints of unspecified or multifactorial etiology such as headache, dizziness, sleep problems and skin symptoms, remains a controversial environmental issue. Evidence does not support an association between RF-EMF exposure and such non-specific symptoms (NSS) in the general population (Röösli et al., 2010a; Baliatsas et al., 2012a; Klaps et al., 2016) as exposure levels in everyday life are documented to be very low compared to the established safety thresholds (ICNIRP, 1998). One of the exposure sources under debate is mobile phone base station(s) (MPBS), the increasing installation of which has been amplifying people's concerns regarding a possible adverse impact on health, especially of those living in the vicinity of such sources (Blettner et al., 2009).

Part of the debate concerns a population subgroup reporting high sensitivity to particular EMF sources/frequencies or EMF in general and who may experience NSS when exposed to levels well below safety thresholds (ICNIRP, 1998). This condition is known as electromagnetic hypersensitivity or idiopathic environmental intolerance attributed to EMF (IEI-EMF) (Hillert et al., 2006). Given the lack of a biological mechanism (Rubin et al., 2011; Augner et al., 2012), symptom attribution and self-reported sensitivity to EMF constitute, at the moment, the cornerstone of IEI-EMF case definition in research and clinical practice (Baliatsas et al., 2012b).

Current conclusions on symptomatic effects of RF-EMF rely to a great extent on findings from experimental studies of small samples, which cannot assess long term effects of real-life exposure conditions (Röösli et al., 2010a; Klaps et al., 2016). Observational research overcomes these limitations, but the number of undertaken studies remains relatively small, while the majority of them are of cross-sectional design (Baliatsas and Rubin, 2014), which does not allow establishment of temporal sequence and investigation of exposure-outcome patterns over time.

Furthermore, health outcome assessment based on medical registry data from general practices was only recently introduced in this research field (Baliatsas et al., 2015). Such data are representative of features of the average patient in primary care and their use minimizes the chance of missing information, loss to follow-up, selection bias and outcome misclassification (Yzermans et al., 2009). Especially when it comes to NSS, the judgment of a general practitioner (GP) can most efficiently determine whether a symptom is associated with known pathology or not (Okkes et al., 2002; van den Berg, 2007;Yzermans et al., 2009).

This study makes an endeavor to fill some of the gaps in the literature, by combining a longitudinal approach with assessment of GP-registered NSS in relation to RF-EMF exposure from MPBS. Two main objectives are addressed: 1) To explore a possible change in prevalence of GP-registered NSS among people living in the vicinity of MPBS, after a period of >6 years, 2) To investigate the effect of RF-EMF exposure from MPBS on NSS after the increase of MPBS antennas in the vicinity of participants' residences.

2. Methods

2.1. Participants and procedure

The present retrospective cohort study was based on general practitioner (GP)-registered data on NSS from two time periods: 1) January–December 2004 (T0 = baseline period) 2) July 2010 and June 2011 (T1 = study period).

Data for T1 were obtained from the database of a large risk assessment study on EMF and non-specific physical symptoms conducted in the Netherlands in 2011 (Baliatsas et al., 2015). This combined a survey questionnaire with data from the electronic health records (EHR) of adult citizens registered in general practices in different areas nationwide. Practices were selected from the primary care database (PCD) of the Netherlands Institute for Health Services Research (NIVEL). Since all Dutch citizens are listed in a general practice, the EHR kept by GPs provides the most detailed picture of population's health (van der Lei et al., 1993). Symptoms and morbidity are coded by GPs in line with the international classification of primary care (ICPC) (Lamberts and Wood, 1987). Consultations regarding the same health problem were grouped into "episodes of care", which are defined as all encounters for the management of the same health problem within a specific period (WONCA, 1995).

Data for the baseline period were collected retrospectively, based on a number of criteria relevant to the aims of the current study: 1) Availability of complete EHR data 2) Symptom data were comparable to those of T1 in terms of registration methodology and episode construction 3) Each participant had been living in the same house at both T0 and T1. The combination of these criteria resulted in a sample of n = 1069 participants (Fig. 1).

The NIVEL PCD is registered with the Dutch Data Protection Authority. According to the Dutch Medical Research Involving Human Subjects Act, ethical approval was not required for this study. Further details regarding the 2011 study design and sampling process are described in previous publications (Baliatsas et al., 2014, 2015).

2.2. Outcome assessment

A selection was made of 27 GP-registered symptoms from multiple organ systems, often presented in general practice as "medically unexplained" (Yzermans et al., 2016). One-year prevalence of NSS was based on care episodes; an episode was defined as "non-specific" if there was no registered diagnosis for an investigated symptom within the examined periods (Biermans et al., 2008).

In terms of outcome operationalization in the present study, symptoms were clustered based on the corresponding organ systems (Table 1). Apart from dividing NSS into organ systems, an additional cluster was created, including symptoms frequently investigated in the peer-reviewed epidemiological literature as theoretically relevant to EMF exposure and highly prevalent among people with IEI-EMF (Baliatsas et al., 2014 and Röösli et al., 2010a); these were: Headache, dizziness or feeling light-headed, nausea, fatigue/tiredness, sleep problems, pain/pressure in chest, memory/concentration problems, skin symptoms, tingling, heart palpitations and ear symptoms.

2.3. Exposure assessment

In this study, we focused on the average residential RF-EMF exposure emitted from different types (GSM900, GSM1800, UMTS) of MPBS. For T1, exposure representative for this period was determined, following the extensively validated approach of the ECOLOG Institute (Neitzke et al., 2007). Calculations (on the power flux density scale) were based on antenna-registry data provided by the Dutch "Antennebureau" (Radio communications Agency Netherlands), which

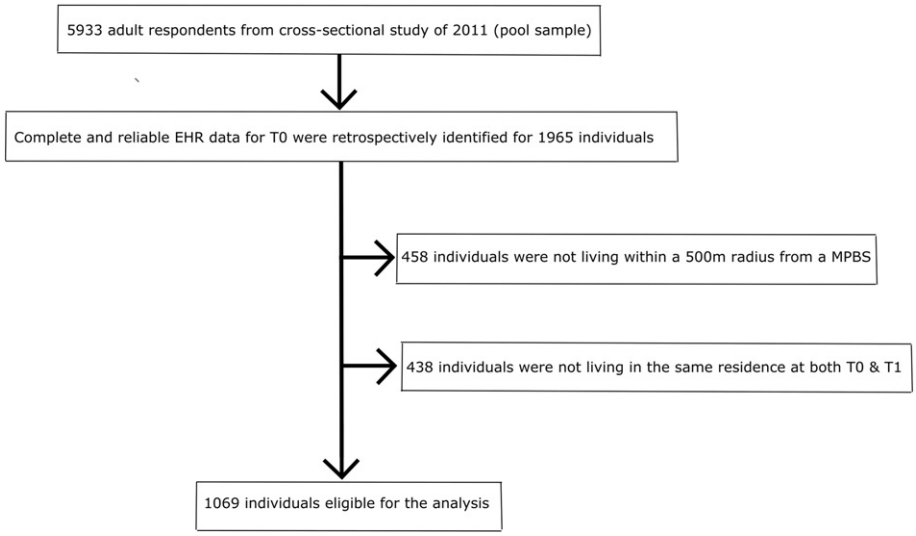


Fig. 1. Schematic illustration of the sample selection.

is the information agency of the Dutch government concerning antennas. This registry contained a complete dataset on location, type and characteristics of the MPBS antennas. For each participant, all base stations within a 500 m radius of the house were identified based on a geographic information system (GIS). Additional information was obtained from the survey questionnaire in 2011 regarding the neighborhood characteristics, orientation of the dwelling and building properties (Kelfkens et al., 2012). Exposure was calculated separately for each frequency band (GSM900, GSM1800, UMTS). The total exposure to MPBS was calculated as the sum of these three exposures. Using an external dataset from Bolte and Eikelboom, 2012, Spearman correlation between maximum measured exposure at night and the current Ecolog model was 0.45 (GSM900), 0.21 (GSM1800) and 0.34 (UMTS). More details regarding the calculation of the ECOLOG model in the present study have been described elsewhere (Kelfkens et al., 2012; Baliatsas et al., 2015).

Baseline information was not available for the years before 2010, regarding the location and characteristics of the antennas. To obtain an estimate of the exposure of a participant at T0 we therefore recalculated the exposure of each individual to GSM900, GSM1800 and UMTS based on the number of these antennas at T1 and T0 (Appendix A). The underlying assumption was that at a given frequency, exposure from MPBS is proportional to the number of antennas at this frequency.

Table 1
Overview of selected GP-registered NSS in the present study and symptom clustering per organ system.

Non-specific symptoms (NSS)	Organ systems
Fatigue/tiredness[a]	General and unspecified
Abdominal/stomach pain Nausea[a] Diarrhea or constipation Weight change	Digestive, metabolic & nutritional
Eye irritation	Eye
Ear symptoms[a]	Ear
Pain or pressure in chest[a] Heart palpitations/awareness[a]	Cardiovascular
Pain in muscles Back problems Arm/elbow/hand/wrist symptoms Neck- or shoulder symptoms Leg/hip/knee/ft symptoms	Musculoskeletal
Headache[a] Tingling of fingers, feet or toes[a] Dizziness or feeling light-headed[a]	Neurological
Feeling anxious/nervous/tense Acute (intense) stress or crisis Feeling down/depressed Feeling irritable/angry Sleep problems[a] Memory- or concentration problems[a]	Psychological
Cough Nasal symptoms Shortness of breath or wheezing	Respiratory
Skin symptoms[a]	Skin

Abbreviations: GP, General practitioner.
[a] Symptoms included in an additional cluster, labeled as "EMF-relevant NSS".

2.4. Case-definition for self-reported sensitivity to mobile phone base stations

Respondents who in 2011 reported "quite agree" or "strongly agree" on the statement: "I am sensitive to mobile phone base stations and devices related to communication systems" were considered as being MPBT-sensitive.

2.5. Demographics

Information on age/date of birth, gender, and home ownership status was based on self-reported data from the 2011 survey.

2.6. Statistical analysis

Descriptive analyses were carried out to produce an overview of sample characteristics and exposure levels at T0 and T1. Differences between

Table 2
Number of antennas and estimated exposure to RF-EMF from MPBS at T0 and T1.

Antenna type (RF-band)	Number of antennas/mean exposure levels V/m (SD)	
	T0	T1
GSM900	6334/0.084 (0.15)	9274/0.102 (0.18)
GSM1800	8943/0.066 (0.17)	3889/0.044 (0.11)
UMTS	1992/0.022 (0.036)	9993/0.05 (0.08)
Total number/total exposure	17,269/0.109 (0.23)	23,156/0.121 (0.22)

Abbreviations: SD, Standard deviation.; MPBS, Mobile phone base stations.

the MPBS-sensitive group and the rest of the sample were assessed with the Fisher's exact test and the unpaired samples *t*-test. McNemar's test was used to assess changes in the prevalence and number of NSS between T0 and T1. Changes in prevalence and number of NSS in relation to exposure over time were investigated by means of multilevel, repeated-measurement logistic and (zero-inflated) Poisson regression analyses respectively, taking into account the hierarchical structure of the data (measurement period: level 1, nested within patients: level 2, nested within general practices: level 3; at the patient level the correlation between measurement periods within patients was modeled as the covariance between these two periods to capture this dependence). Exposure–outcome associations were analyzed separately for each exposure variable. Analyses were adjusted for participants' date of birth (continuous), gender and house ownership status (owned vs. rented).

In addition, to test whether the exposure-outcome associations differ between MPBS-sensitive and non-sensitive individuals (reference group), the regression models were extended with the inclusion (one at a time) of an interaction term (MPBS-sensitive group × RF-EMF exposure estimate).

For each investigated association, Odds ratios (OR) or incidence rate ratios (IRR) and 95% confidence intervals (CI) were computed. A p value of <0.05 was considered statistically significant. Analyses were performed with STATA version 13.0 (StataCorp LP, College Station, TX, USA) and MLwiN version 2.30 (Centre for Multilevel Modelling, University of Bristol, Bristol, UK).

3. Results

3.1. Sample characteristics

Details regarding the number of MPBS in the study areas at T0 and T1 and the corresponding calculated RF-EMF exposure levels are shown in Table 2. There was an increase in the total number of antennas of >30% compared to T0. The change in numbers of antennas differed per antenna type. For UMTS antennas there was a fivefold increase at T1. For GSM900 the increase was about 45%. In contrast, the number of GSM1800 antennas at T1 was reduced about 55%. Mean (SD) total RF-EMF for the MPBS-sensitive group was 0.10 (0.15) V/m at T0 and 0.104 (0.15) at T1; for the rest of the sample mean exposure levels were 0.11 (0.23) V/m and 0.12 (0.23) respectively.

Demographic and symptom characteristics of the total sample and the MPBS-sensitive group (5.2%) are provided in Table 3 and Table 4 respectively. Symptoms in the musculoskeletal cluster had the highest prevalence in both groups and at both time periods.

Individuals that were excluded from the analyses due to the eligibility criteria (Fig. 1) were generally younger (mean 51.1 years at T1, p < 0.00) and more often female (60%, p < 0.00) and MPBS-sensitive (6.9% at T1, p < 0.05) compared to the included sample. Furthermore, they owned their house less often (63%, p < 0.00). Nevertheless, there was no significant difference in prevalence of GP-registered NSPS (37.9% for the excluded individuals, p > 0.05).

3.2. Association between RF-EMF from base stations and symptoms

Results of the primary analysis are summarized in Table 5. No significant association between the examined symptoms and RF-EMF exposure from MPBS was found in the sample.

3.3. Interaction analysis

Most of the tests did not yield a significantly higher risk of NSS for the MPBS-sensitive group in relation to exposure, compared to the rest of the sample (data not shown). However, statistically significant positive interactions were observed between MPBS-sensitivity and exposure to UMTS on risk of neurological symptoms (OR = 2.34, 95% CI: 1.19–4.59, p = 0.01), respiratory symptoms (OR = 2.38, 95% CI: 1.18–4.76, p = 0.01), EMF-relevant NSS (OR = 2.0, 95% CI: 1.05–3.8, p = 0.03), and number of NSS (IRR = 1.46, 95% CI: 1.17–1.83, p < 0.001). Also the association between ear symptoms and GSM900 (OR = 7.4, 95% CI: 1.45–37.6, p = 0.01) and total RF-EMF exposure from MPBS (OR = 7.6, 95% CI: 1.39–41.6, p = 0.02) was stronger for the MPBS-sensitive participants.

Table 3
Demographic and symptom characteristics of the study population (n = 1069)[a].

Characteristics[b]	T0	T1
Mean age (SD)		57.4 (14.7)
Female gender, % (n)		51.6
Home ownership status (owned), % (n)		74.8
Total prevalence of NSS, % (n)	37.3 (399)	36.5 (390)
Mean number of NSS (SD)	0.55 (0.87)	0.54 (0.86)
EMF-relevant NSS, % (n)	13.1 (140)	15.3 (164)
Symptom categorization/clusters per organ system, % (n)		
Fatigue/tiredness	2.1 (22)	2.6 (28)
Digestive & metabolic/nutritional	6.2 (66)	7.4 (79)
Eye irritation	0.5 (5)	0.5 (5)
Ear symptoms	**1.0 (11)**	**2.1 (22)**
Cardiovascular symptoms	3.7 (39)	3.8 (41)
Musculoskeletal symptoms	**20.1 (220)**	**17.3 (185)**
Neurological symptoms	3.5 (37)	3.9 (42)
Psychological symptoms	6.6 (70)	5.9 (63)
Respiratory symptoms	5.0 (53)	5.3 (57)
Skin symptoms	0.7 (7)	1.3 (14)

Abbreviations: GP, General practitioner; NSS, Non-specific symptoms; SD, Standard deviation.
In bold: Significant differences between T0 and T1 at p < 0.05.
[a] There were no missing values except for the variable "home ownership status" (n = 5).
[b] Demographic characteristics were obtained from the 2011 survey.

4. Discussion

4.1. Primary findings

The present study examined the prevalence of NSS registered in general practices, before and after an increase in the number of MPBS antennas, with a time difference of >6 years. Compared to the baseline

Table 4
Demographic and symptom characteristics of the MPBS-sensitive group (n = 55)[a].

Characteristics[b]	T0	T1
Mean age (SD)		58.3 (13.9)
Female gender, % (n)		67.3
Home ownership status (owned), % (n)		69.1
Total prevalence of GP-registered NSS, % (n)	34.6 (19)	49.1 (27)
Mean number of NSS (SD)	**0.47 (0.74)**	**0.8 (1.0)**
EMF-relevant NSS, % (n)	16.4 (9)	27.3 (15)
Symptom categorization/clusters per organ system, % (n)		
Fatigue/tiredness	3.6 (2)	5.5 (3)
Digestive	5.5 (3)	7.3 (4)
Eye irritation	1.8 (1)	1.8 (1)
Ear symptoms	0.0 (0)	5.5 (3)
Cardiovascular symptoms	5.5 (3)	3.6 (2)
Musculoskeletal symptoms	18.2 (10)	21.8 (12)
Neurological symptoms	5.5 (3)	3.6 (2)
Psychological symptoms	**1.8 (1)**	**12.7 (7)**
Respiratory symptoms	0.0 (0)	9.1 (5)
Skin symptoms	0.0 (0)	5.5 (3)

Abbreviations: MPBS, Mobile phone base stations; NSS, Non-specific symptoms; SD, Standard deviation.
In bold: Significant differences between T0 and T1 at p < 0.05.
[a] There were no missing values.
[b] Demographic characteristics were obtained from the 2011 survey.

Table 5
Results of the multilevel analyses[a] on the association between the investigated outcomes and (per frequency band and total) exposure.

Outcomes	Estimates of RF-EMF exposure from MPBS			
	GSM900	GSM1800	UMTS	Total exposure
OR (95% CI)				
Total prevalence of NSS	0.93 (0.83–1.05)	1.09 (0.93–1.26)	0.91 (0.81–1.01)	0.99 (0.9–1.09)
EMF-relevant NSS	1.00 (0.88–1.12)	1.08 (0.97–1.2)	0.95 (0.82–1.09)	1.04 (0.94–1.15)
Symptoms/clusters per organ system				
Fatigue/tiredness	0.99 (0.79–1.26)	0.94 (0.62–1.44)	1.00 (0.77–1.28)	0.98 (0.75–1.27)
Digestive & metabolic/nutritional	0.81 (0.59–1.11)	0.98 (0.78–1.23)	0.73 (0.52–1.03)	0.81 (0.56–1.18)
Ear symptoms	0.83 (0.46–1.53)	0.9 (0.35–2.3)	0.96 (0.68–1.37)	0.83 (0.4–1.72)
Cardiovascular symptoms	0.96 (0.72–1.27)	0.67 (0.28–1.6)	0.87 (0.6–1.24)	0.88 (0.57–1.36)
Musculoskeletal symptoms	0.88 (0.74–1.04)	0.98 (0.87–1.1)	0.98 (0.86–1.1)	0.92 (0.77–1.09)
Neurological symptoms	1.05 (0.91–1.21)	1.1 (0.99–1.24)	1.0 (0.81–1.23)	1.09 (0.98–1.21)
Psychological symptoms	0.96 (0.78–1.18)	0.95 (0.74–1.22)	0.92 (0.72–1.16)	0.95 (0.75–1.2)
Respiratory symptoms	0.99 (0.8–1.22)	1.02 (0.87–1.2)	0.96 (0.76–1.2)	1.00 (0.82–1.23)
Skin symptoms	1.02 (0.75–1.39)	1.07 (0.93–1.24)	0.92 (0.55–1.53)	1.06 (0.86–1.31)
IRR (95% CI)				
Number of NSS	0.94 (0.86–1.03)	1.01 (0.96–1.06)	0.92 (0.84–1.01)	0.96 (0.88–1.06)

Abbreviations: MPBS, Mobile phone base stations; NSS, Non-specific symptoms; OR, Odds ratios; CI, Confidence intervals; IRR, Incidence rate ratios.
[a] Adjusted for date of birth, gender, house ownership status.

period, there was a higher prevalence of symptoms theoretically relevant to EMF at T1. A significant increase was observed in the prevalence of ear symptoms and a two-fold (but not significant) increase in the prevalence of skin symptoms. Overall, the total prevalence of GP-registered NSS was slightly lower at T1. No association was found between NSS and modeled exposure from MPBS in the total sample. This is in line with evidence from the only study of longitudinal design that has been previously published in the peer-reviewed literature (Frei et al., 2012; Mohler et al., 2012). Current results also corroborate those of recent cross-sectional studies and double-blind experiments, showing no effects of MPBS exposure on symptoms (Röösli et al., 2010a; Klaps et al., 2016). The estimated mean values of total exposure levels at T1 were much lower than the established safety thresholds in the general population (ICNIRP, 1998) but generally higher than other recent epidemiological studies on exposure from fixed transmitters (Mohler et al., 2010).

4.2. Self-reported sensitivity to MPBS

In the MPBS-sensitive group, most symptom clusters were more prevalent at T1 compared to baseline, particularly those in the psychological and EMF-relevant cluster.

A number of statistically significant differences were observed between MPBS-sensitive and non-sensitive individuals regarding the exposure-outcome associations. Since the interaction analyses were based on a relatively small number of MPBS-sensitive people, they are primarily exploratory and the results must be interpreted with caution.

An earlier longitudinal investigation focusing on a similar group (Röösli et al., 2010b) found some significant associations between exposure and self-reported symptoms, which were attributed to chance due to the lack of consistency and large number of statistical tests; the latter was the case in this study as well. In addition, since self-reported data were not available at baseline, we did not adjust for the possible effect of perceived exposure, which reflects the individual belief of being exposed to EMF. Considering its importance as a psychosomatic determinant of symptom report and duration (Baliatsas et al., 2015) and that a substantial part of individuals with IEI-EMF claims to be able to perceive exposure (Röösli et al., 2004), it is possible that perceived exposure accounted, at least partly, for the observed effects. The noteworthy increase at T1 of psychological complaints among MPBS-sensitive participants might be supportive of that notion, the mere introduction of an environmental stressor in the residential vicinity and media attention for it, can have a negative influence on residents' health perceptions (Porsius et al., 2015).

Despite these important considerations, the present study showed a consistent association between UMTS exposure and different clusters of GP-registered symptoms, for the self-declared MPBS-group. Furthermore, the cross-sectional investigation of 2011 using estimates of personal RF-EMF and a larger sample of sensitive individuals, found sporadic significant sensitivity-exposure interactions, controlling for perceived exposure (Baliatsas et al., 2015). Thus, it cannot be entirely excluded that the observed interactions do indicate an actual exposure effect, especially given the limited research on detrimental effects of everyday life EMF exposure on potentially susceptible population subgroups. These findings should be verified in future studies.

4.3. Strengths and limitations

This is the first epidemiological study in this field combining a before-after approach with well-defined outcome variables based on a reliable registration system (Okkes et al., 2002). Additional strengths are the long latency period between T1 and T0 that in principle optimizes exposure contrast, the large sample size and the solid outcome assessment including multiple symptoms and clusters of symptoms.

A number of limitations must be reported. In terms of exposure assessment, no data on location and characteristics of base station antennas were available for the baseline period, but only the number and type of installed antennas. Regarding T1, the antenna dataset did not contain detailed information on the tilt of each antenna separately and therefore a fixed tilt was used. The ECOLOG model does not encompass indoor signal propagation. Because the 2011 questionnaire focused on the bedroom, only bedroom exposure at T1 was modeled. Limitations in the input data can introduce misclassification and reduce the accuracy of exposure prediction (Beekhuizen et al., 2014a). Studies comparing personal exposimeter measurements with modeled exposure in the bedroom using NISmap, found a moderate Spearman correlation between model predictions and personal 24-h of 0.36 (Martens et al., 2015) and personal 48-h of 0.47 (Martens et al., 2015).

Furthermore, analyses were only adjusted for a basic set of potential confounders; determinants of NSS within the EMF context such as perceived exposure (Baliatsas et al., 2015) were not taken into account. Low study power in relation to the MPBS-sensitive group and simplified case definition in view of the absence of established diagnostic criteria comprise additional shortcomings. Finally, outcome assessment was based on one-year prevalence which does not necessarily indicate symptom persistence. Thus, we may have missed patients with persistent NSS whose symptom was not registered within the examined timeframes.

The abovementioned shortcomings should be addressed in future studies. Especially characterization of exposure remains one of the

major methodological challenges in this research field, since misclassification can be introduced even when employing state-of-the-art measures (Bolte et al., 2011, Bolte and Eikelboom, 2012). Recently developed geospatial models based on detailed three-dimensional neighborhood data constitute a cost-efficient improvement of the older propagation models and a reliable representation of everyday life exposure to RF-EMF (Beekhuizen et al., 2014b, Martens et al., 2015). Due to the retrospective nature of our study, it was not possible to determine whether participants who claimed to be sensitive in 2011 were already sensitive in 2004 or that sensitivity developed after the introduction and gradual increase of MPBS in the vicinity of their residence.

Future cohort studies should be able to expand the standard risk assessment approach by monitoring the development of sensitivities and associated symptoms in relation to exposure over a long period of time, while taking into account predisposing, precipitating and maintaining factors of symptomatic conditions related to the environment.

5. Conclusions

In conclusion, this before-after study found no evidence that RF-EMF exposure from mobile phone base stations is associated with the development of NSS in the general population, corroborating recent observational studies. Subgroup analyses among people with self-reported sensitivity to base stations showed a higher prevalence for most symptoms at T1 compared to baseline and there was some indication for a higher risk of NSS for the MPBS-sensitive group, in relation to exposure. Future epidemiological research on EMF and health should focus more on potentially susceptible population subgroups, including people with self-declared sensitivity to EMF sources.

Competing interests statement

The authors have no competing interests to report.

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Appendix A. Calculation of RF-EMF exposure from MPBS at T0

$$exposure(GSM900, T0) = \frac{number of\ GMS900\ antennas\ at\ T0}{number of\ GSM900\ antennas\ at\ T1} \times exposure(GSM900, T1.)$$

$$exposure(GSM1800, T0) = \frac{number of\ GMS1800\ antennas\ at\ T0}{number of\ GSM1800\ antennas\ at\ T1} \times exposure(GSM1800, T1)$$

$$exposure(UMTS, T0) = \frac{numberofGUMTSantennas\ at\ T0}{numberofUMTSantennas\ at\ T1} \times exposure(UMTS, T1)$$

$$totalexposure(T0) = dose\ (GSM900, T0) + dose(GSM1800, T0) + exposure(UMTS, T0)$$

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