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Comparing non-specific physical symptoms in environmentally sensitive patients: Prevalence, duration, functional status and illness behavior

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ABSTRACT

Objective: Little is known about the potential clinical relevance of non-specific physical symptoms (NSPS) reported by patients with self-reported environmental sensitivities. This study aimed to assess NSPS in people with general environmental sensitivity (GES) and idiopathic environmental intolerance attributed to electromagnetic fields (IEI-EMF) and to determine differences in functional status and illness behavior.

Methods: An epidemiological study was conducted in the Netherlands, combining self-administered questionnaires with the electronic medical records of the respondents as registered by general practitioners. Analyses included n = 5789 registered adult (≥ 18 years) patients, comprising 5073 non-sensitive (NS) individuals, 514 in the GES group and 202 in the IEI-EMF group.

Results: Participants with GES were about twice as likely to consult alternative therapy compared to non-sensitive individuals; those with IEI-EMF were more than three times as likely. Moreover, there was a higher prevalence of symptoms and medication prescriptions and longer symptom duration among people with sensitivities. Increasing number and duration of self-reported NSPS were associated with functional impairment, illness behavior, negative symptom perceptions and prevalence of GP-registered NSPS in the examined groups.

Conclusion: Even after adjustment for medical and psychiatric morbidity, environmentally sensitive individuals experience poorer health, increased illness behavior and more severe NSPS. The number and duration of self-reported NSPS are important components of symptom severity and are associated with characteristics similar to those of NSPS in primary care.

The substantial overlap between the sensitive groups strengthens the notion that different types of sensitivities might be part of one, broader environmental illness.

INTRODUCTION

People often experience symptoms such as headaches, fatigue, musculoskeletal pain, sleep problems and bowel disturbances, which are not necessarily related to a medical condition. More than 80% of the general population experiences at least one of such non-specific physical symptoms (NSPS) in any given month [1] and [2]. When presented to the general practice (GP), between 30% and 50% of NSPS cannot be sufficiently explained by a pathological cause and are often labeled as medically unexplained [3] and [4]; according to more recent evidence, these rates can be even higher [5]. However, the term “medically unexplained” is perceived as negative by patients [6] or ambiguous, connoting that the health provider is not able to help or that the symptoms can only be psychiatrically explained [7]. For these reasons and considering that such symptoms are usually reported in different organ systems [8], the term NSPS will be used in the following. In medical care, NSPS are associated with functional impairment similar to that of patients with medical disorders [9], increased illness behavior [10], high levels of psychological distress [11] and [12] and negative symptom perceptions [13] and [14].

Experiencing NSPS is a main characteristic of self-declared sensitivities attributed to low (in relation to established effect thresholds) levels of exposure to environmental agents such as electromagnetic fields (EMF). However, there is no convincing evidence for a causal dose–response association and a broadly accepted case definition for patients is missing [15], [16], [17], [18], [19], [20], [21] and [22]. Although not well-established, there is the notion that self-reported sensitivity to EMF sources, described by the WHO as idiopathic environmental intolerance attributed to EMF (IEI-EMF) [23] and other diverse environmental sensitivities, such as those to odorous chemicals, food additives and noise, may constitute dimensions of just one condition; a generalized environmental sensitivity which is usually referred to as idiopathic environmental intolerance (IEI) [24], [25], [26] and [27]. This notion is mainly based on evidence that patients tend to be sensitive to more than one environmental sources [28] and [29] and the lack of symptom patterns [28]; IEI has been considered as part of the broader spectrum of functional somatic syndromes [12] and can co-occur with syndromes such as fibromyalgia and chronic fatigue [30]. However, evidence on the clinical pertinence of symptoms reported by environmentally sensitive individuals is still scarce. Important information regarding the clinical profile of the patients such as prevalence of registry-based medical and psychiatric morbidity and prescribed medication is also missing at the population level.

On the one hand, only a diagnostic evaluation could sufficiently determine whether underlying pathology accounts for the symptoms [31] and [32]. On the other hand, persistent presentation of NSPS to the GP is relatively rare [33], [34] and [35] and patients who seek health care are not always those with increased functional impairment [32], [36], [37] and [38]. This means that a large pool of symptomatic cases in the population has not been studied in primary care research [39]. Evidence from studies in the general population and among disaster survivors suggests that

NSPS reported in surveys share several features with NSPS in medical care, showing that increased number of self-reported NSPS is a strong indicator of functional impairment and illness behavior [2] and [7]. However, it is not clear yet whether this is the case for NSPS reported by individuals with environmental sensitivities, such as IEI-EMF and the broader condition of IEI. Additional components of symptom severity, such as duration, should also be considered to understand the clinical importance of symptomatology [32].

The following research questions were addressed in the present study: 1) Do people with IEI-EMF and those with general environmental sensitivity experience more NSPS and NSPS of longer duration compared to participants without such sensitivities? 2) Do the examined groups differ in terms of symptom patterns, functional status and illness behavior? 3) What is the association between self-reported NSPS and functional impairment, illness behavior and GP-registered NSPS among sensitive and non-sensitive individuals?

METHODS

Study design and participants

Data were collected within the framework of an epidemiological study into NSPS in relation to actual and perceived exposure to EMF (EMPHASIS). The study was carried out between January 21 and 23 June 2011 in the Netherlands, combining self-administered questionnaires and electronic medical records (EMR) of health problems, registered in GPs within the Dutch Information Network of General Practices (LINH) [40]; every Dutch citizen is obliged to be registered at one GP, so the population listed in family practice can be used as the denominator in epidemiological studies [40], [41] and [42]. Data collection within the LINH network is carried out according to the Dutch legislation on privacy. Each patient is coded with an anonymous administrative number. The key to this coding number is only with the general practitioner. The privacy regulation of the study was approved by the Dutch Data Protection Authority. Based on the Law on Medical Scientific Research (WMO), the Dutch Medical Ethics Committee decided that an ethical approval was not required.

Twenty-one practices, varying in terms of number of patients and level of urbanization were selected from the primary care database of the Netherlands Institute for Health Services Research (NIVEL). Registered patients were listed according to postal codes and house number; a geographical information system (GIS) layer of these addresses was then created, resulting to a total pool of 76,684 eligible addresses. A random sample among the adult population (≥ 18 years) was drawn from the GP registry data set, initially stratified by age, gender and preliminary estimates of EMF exposure from mobile phone base stations [43]. Only one adult was sampled from each household. All invitees ($n = 13,007$) received a letter from their GP to fill out a questionnaire, either electronically or in a paper version, entitled "Living environment, technology and health", along with an information leaflet and informed consent form. If a completed questionnaire had not been received, a reminder letter was sent two weeks after the first invitation and a second reminder two weeks later. This resulted in $n = 5933$ respondents (response rate: 46%). Twenty percent of the respondents filled out the survey online. A non-

response follow-up on a shorter version of the questionnaire was also conducted, including $n = 505$ individuals.

Case definitions

Selection of individuals with IEI-EMF was based on findings from a recent systematic evaluation of the relevant literature [21], considering that: 1) IEI-EMF is a highly heterogeneous condition in terms of severity and associated EMF sources; 2) self-reported (hyper) sensitivity to EMF is the most often used criterion for patient identification in the literature; 3) most people with IEI-EMF tend to be sensitive to more than one EMF source. Therefore, two items were used to assess IEI-EMF in the study sample, asking the extent to which people agree with the following statements:

1) "I am sensitive to mobile phone base stations and devices related to communication systems (e.g. mobile phones, wireless internet etc.)" and 2) "I am sensitive to electrical devices (e.g. domestic appliances etc.)"; answers were scored on a five-point scale, ranging from "strongly disagree" to "strongly agree". Those who indicated "quite agree" to "strongly agree" were included in the IEI-EMF group.

A list of nine items assessing sensitivity to several environmental stressors (other than EMF) such as chemical substances, smells in general and in relation to scented detergents, noise, light, various materials, color, temperature changes and cold or warm environment was used to assess general environmental sensitivity (GES), adapted from Stansfeld et al. [44]. Answers were scored in a similar format as the items on IEI-EMF mentioned above. Respondents with a score at or above the 90th percentile of the score distribution (which corresponds to an average per-item response of at least "quite agree"), were included in the GES group. Participants who had more than one items missing were excluded from subsequent analyses.

Assessment of self-reported non-specific physical symptoms (NSPS)

To assess NSPS, 23 items from the recently developed Symptoms and Perceptions (SaP) scale [45] were selected. These correspond to physical symptoms similar to those reported by patients in general practice, based on the International Classification of Primary Care (ICPC-1) [46]. The included items ask respondents on a binary scale whether they experienced any of the examined symptoms in the past month; if so, respondents are asked about how long they have been bothered by these symptom(s), with responses formed on a 5-point scale, with "over 6 months" as the highest value. A higher total score in the corresponding characteristics indicates increased number of NSPS and related duration (Internal consistency based on the total analyzed sample: Cronbach's $\alpha = .80$ for and $\alpha = .82$ respectively).

Moreover, the sum scores were added together and categorized into four ranges, based on the approach of van den Berg et al. [7], to present more explicitly the relationship between graded increases in NSPS and the different indicators of functional status and illness behavior: The first range was 0 to 1 symptom, the second 2 to 9 symptoms, the third 10–14 symptoms and the fourth 15 or more symptoms. Following similar methodology, the total score on duration was

categorized into 4 ranges as well, corresponding to different percentiles (> 50th, 50th–79th, 80th–94th and 95th), based on the distribution reported by the NS group.

Assessment of GP-registered NSPS

Non-specific physical symptoms in EMR were registered by the GP according to the ICPC-1 [46]. The evaluation of the clinical judgment of the GP on the symptoms was based on “episodes of care”, representing the period from the first presentation of a health problem to a general practice until the completion of the last encounter for the same problem [47]. An episode was defined as “non-specific” if no medical diagnosis had been registered as an explanation for the symptoms, during the year before the completion of the present study. In order to evaluate the association between self-reported and registry based NSPS, we compared the 23 self-reported NSPS with potentially corresponding NSPS in the medical records of the participants [7]. For example, the symptom “headache” corresponded to the ICPC codes N01 (headache) and N02 (tension headache). The total prevalence of registered-NSPS was treated as a dichotomous variable.

Assessment of functional status

For the same period, the GP-registered prevalence of prescriptions related to painkillers, tranquilizers (benzodiazepines) and antidepressants were examined, classified according to the Anatomical Therapeutic Chemical Classification system (ATC) [48].

Participants also completed the General Health subscale of the RAND-36 Health Survey questionnaire [49], which is scored from 0 to 100. A higher score represents better physical functioning.

Sleep quality was assessed using a 10-item version of the Groningen Sleep Quality Scale (GSQS) [50] and [51]. Answers were formatted on a binary scale, with a higher sum score demonstrating lower self-reported sleep quality. Psychological distress was assessed with the 12-item version of the General Health Questionnaire (GHQ-12) [52], [53] and [54]. The 4-point Likert-type scoring method was used in the present analyses; a higher total item score indicates increased distress.

Measures of illness behavior and symptom perceptions

Participants were asked whether they consulted a GP, a psychologist/psychotherapist and/or an alternative therapist (e.g. homeopathist, acupuncturist or paranormal therapist) and also whether they used any unprescribed medication within the past year.

Symptom perceptions were assessed using the items related to consequences and emotional response of the Brief Illness Perceptions Questionnaire (Brief-IPQ) [55] and [56]. The items were scored on a 10-point Likert scale and referred to the symptom perceived as the most important. Higher scores indicate a greater perceived influence of the reported symptom on life and a stronger, negative emotional response.

Finally, information was obtained on socio-demographic characteristics, lifestyle indicators and GP-registered (based on the ICPC-1) medical (co)morbidity and psychiatric (co)morbidity.

Data analysis

To examine potential differences between the three groups in terms of symptom report, functional status, illness behavior and symptom perceptions, linear (for the continuous outcomes) and logistic (for the dichotomous outcomes) regression analyses were used to control for socio-demographic characteristics and medical and psychiatric morbidity. None of the examined continuous scores exceeded the suggested acceptable values for skewness [57]. No risk for multicollinearity was observed. Analysis of variance (one-way ANOVA), the chi-squared test, Cramer's V, and the unpaired samples *t*-test were performed for the descriptive analyses and to examine the associations between symptom categories and indicators of functional status, illness behavior and perceptions. Depending on the type of analyzed variables, effect sizes (regression coefficient, ORs, Cramer's V statistic, Pearson *r* coefficient) are presented for the main results. The non-parametric equivalent of the ANOVA (Kruskal–Wallis test) was employed to verify the consistency of the findings. To determine whether medical morbidity affected the results, analyses were repeated for participants without registered medical conditions. Post-hoc comparisons were also performed to verify differences between the symptom groups, using the Games–Howell and Bonferroni procedures [58] and [59]. In all tests, the significance level was set at $p < .05$. When self-reported NSPS were examined as a sum score, respondents who had more than five items on the 23-symptom list missing were excluded from the analyses.

Missing values in the rest of the self-reported measures were treated according to the guidelines or previous publications on these measures. Statistical analyses were carried out using IBM SPSS Statistics (SPSS Inc. version 19, Chicago IL, USA).

RESULTS

Descriptive analyses and non-response

Based on the employed case definition criteria and after exclusion of associated incomplete items ($n = 144$), a total sample of 5789 respondents was available for analysis; $n = 202$ (3.5%) and $n = 514$ (8.8%) met the criteria for the IEI-EMF and GES group respectively, while the rest of the participants ($n = 5073$) formed the “control”, non- (environmentally) sensitive (NS) sample.

Seventy-seven (38%) of participants in the IEI-EMF group also met the criteria for GES. Demographic characteristics, lifestyle indicators and medical and psychiatric morbidity for the three groups are presented in Table 1. Compared to non-respondents, participants in the total sample were younger (mean age 51.8, SD 17.1 versus 55.0 SD 18.9, $p = .001$), higher educated (higher vocational education or university 32% vs. 21.5%, Cramer's V = .096, $p = .00$) and with better perceived health (good, very good or excellent perceived health 82% vs. 73.5%, OR .6, 95% CI .48–.76, $p = .00$).

[TABLE 1]

There was no significant difference in gender distribution (female gender 58% vs. 59.5%, OR 1.05, 95% CI .86–1.29, $p = .61$). Among the non-respondents, 89%

provided reasons for not participating in the study: (26%) stated that they had no time, 22.5% had no interest to participate, 14.5% had no health complaints and 26% provided various other (additional) reasons.

NSPS, functional status and illness behavior: differences between GES, IEI-EMF and controls (NS)

Controls reported a mean number of 5.0 (SD 3.8) NSPS in the past month, which was significantly lower than the mean number of 6.9 (SD 4.5) symptoms in the IEI-EMF group and the mean number of 7.7 (SD 4.5) symptoms in the GES group ($p = .00$). The total prevalence of registry-based NSPS was 35% in the NS group, 42% in the IEI-EMF and 43% in the GES group ($p = .001$).

There was a higher prevalence and longer duration of all self-reported symptoms among people with environmental sensitivities, especially those with GES, compared to the NS group (Table 2 and Table 3, Fig. 1); symptoms in particular organ systems such as the digestive and cardiovascular, were strikingly pronounced in the GES and IEI-EMF group respectively.

[TABLE 3] [FIGURE 1]

Participants in the sensitive groups had higher levels of functional impairment, symptom scores, negative symptom perceptions and illness behavior; the latter was more related to alternative therapies rather than consulting a GP (Table 4).

CSV Association between self-reported NSPS and indicators of functional status and illness behavior

View in workspaceDownload as With increasing number and duration of self-reported NSPS in the three groups, there was an increase in GP-registered NSPS and the examined indicators of functional impairment and illness behavior (Fig. 1, Table 5 and Table 6). Significant associations were verified by post-hoc comparisons (data not shown). In the two environmentally sensitive groups, not all associations reached statistical significance. For instance, although there was a significantly higher prevalence of registered NSPS with increasing number and duration of self-reported NSPS in the NS group (Cramer's $V_{\text{number}} = .17$, $p = .00$ & $V_{\text{dur}} = .21$, $p = .00$) and with increasing symptom duration in the GES group ($V_{\text{number}} = .12$, $p = .07$, $V_{\text{dur}} = .16$, $p = .01$), such associations were not observed for the IEI-EMF group ($V_{\text{number}} = .15$, $p = .3$, $V_{\text{dur}} = .17$, $p = .2$) (Fig. 1). The results of ANOVA did not change after repeating the analyses with non-parametric tests. Overall, the two highest categories of symptom number and duration (≥ 10 and 80th percentile respectively) remained the ones with the highest scores on functional impairment, illness behavior and negative symptom perceptions after exclusion of respondents with medical and psychiatric morbidity (data not shown).

DISCUSSION

The present study focused on NSPS and potentially clinically relevant characteristics among people with and without self-reported environmental sensitivities. Results showed that the IEI-EMF and GES groups were considerably more symptomatic, with more chronic symptoms, higher levels of functional impairment, negative symptom perceptions and illness behavior that was mainly related to psychological and alternative therapies. Effect sizes for these differences remained moderate to

strong, even after adjustment for medical and psychiatric morbidity. Moreover, there were no distinct differences in the prevalence of GP consultations compared to controls, which is in line with recent evidence [60]. Collectively, increasing number and duration of self-reported NSPS were strongly associated with decrease in functional status and moderately associated with increase in illness behavior, negative symptom perceptions and prevalence of GP-registered NSPS; associations were robust across groups, as indicated by the consistency of the reported effect sizes. Results are in agreement with evidence from studies on disaster survivors and community samples [2], [7] and [14].

Almost half of the respondents in the NS group with a range between 10 and 14 self-reported NSPS in the past month, had at least one NSPS in their medical records; this was over 60% for those who experienced 15 or more NSPS. Similar findings were observed for the categories of longer symptom duration. This pattern was less consistent for the GES and IEI-EMF compared to the NS group: The prevalence of registered NSPS dropped at the highest categories of symptom severity, possibly because of the low (given their functional status) rates of medical consultations, while this was not the case for the prevalence of other types of therapies. This might be explained by the fact that the course of idiopathic environmental sensitivities can be chronic, lasting for years [16], [61] and [62]. It is therefore possible that there was an underestimation of the prevalence rates of registered NSPS and/or medication among environmentally sensitive patients because they already consulted their GP for their symptoms and/or follow other types of consultation/therapy.

This is to our knowledge the largest investigation so far on symptom characteristics of people with GES and IEI-EMF in terms of group sizes and health indicator assessment. It is also the first study addressing a wide range of NSPS in terms of both number and duration in combination with GP-registry data of registered NSPS and medication, based on a large primary care database. Although the assessment of self-reported NSPS was based on a recently developed scale, we used it in relation to an extended set of (self-reported and registry based) health indicators, showing a number of associations comparable with studies that used different questionnaires [2], [7] and [63], indicating consistency across various measures. Moreover, the prevalence of registered medical morbidity and anxiety and depressive disorder represents real-life practice and was comparable with 12-month rates from epidemiological studies in the Netherlands and other countries [64], [65], [66], [67], [68] and [69].

In the absence of an established case definition for environmental illnesses [16] and [21], the IEI-EMF and GES group were defined based on a systematic evaluation of the peer-reviewed literature and use of items on several environmental exposures respectively. We used case-definitions that were independent of attributed symptoms, aiming to a more objective investigation of symptom profiles, without predisposing participants through leading questions. The fact that we adjusted for the presence of common medical and psychiatric disorders makes it unlikely that all the between-group differences and the increased symptomatology in the sensitive groups are the result of an unrecognized medical condition, although there is often some comorbidity between medical and/or psychiatric conditions and NSPS [70], [71] and [72].

Some limitations of the study should be acknowledged. The first one is related to the sensitivity and specificity of the ICPC codes, which we used to compare GP-

registered and self-reported NSPS. It is possible that not all symptoms presented by the patients were registered by the GP or the GP used an ICD-10 code that we did not consider as corresponding to the self-reported symptom; these could lead to an underestimation of the prevalence of people with registered NSPS in the sample (false negatives). Second, we defined an episode as “non-specific” if it was not related with a medical diagnosis during the year before the completion of data collection for our questionnaire survey. Although this time interval could be considered sufficient for the investigation of such health outcomes, some of the participants might have been diagnosed with a medical condition a few days or months earlier or after the set timeframe. Finally, despite the large sample, some risk for selection bias cannot be ruled out. Since the overall respondents were healthier than the non-respondents, we may have underestimated the prevalence of symptoms to some degree. However, the response rate of the survey is considered satisfactory and comparable to other studies on residential EMF exposure and NSPS [30]. This study aimed to provide insight into clinically relevant characteristics and symptom features of the examined groups. Taking the current findings into account, the notion that IEI-EMF may be part of a broader condition such as GES (or IEI) could be strengthened, considering: 1) the similarities between the sensitive groups in terms of functional impairment and illness behavior 2) the prominence of neurological symptoms, fatigue and muscular pain in both groups and 2) the fact that approximately 40% of participants with IEI-EMF met the criteria for GES and the rest of this group reported high levels of general sensitivity as well (although lower than the threshold that was used for GES).

While more than 25% in the GES and IEI-EMF group reported ≥ 10 NSPS in the past month, the one-year prevalence of diagnosed somatization disorder and/or neurasthenia was 2.3% and 1.5% respectively. This might imply that undiagnosed somatoform disorders are more pronounced among people with environmental sensitivities, considering the significant overlap demonstrated in clinical investigations [30] and [74] and that existing diagnostic criteria have been criticized for their restrictiveness [73]. However, this seems to be only a part of the spectrum and can be influenced by the methodology of identifying patients with self-reported sensitivities.

Symptoms can occur due to different interrelated factors, psychological and environmental [75]. In the case of IEI-EMF for instance, on the one hand, a bioelectromagnetic mechanism cannot be ruled out completely, given the methodological challenges that experimental and observational research in this field are confronted with [76]. On the other hand, a strong body of experimental evidence suggests that patients tend to experience symptoms when they believe they are being exposed regardless of whether these beliefs are accurate [19] and [77], highlighting the importance of psychological processes [78] and [79]. We therefore suggest that environmental illnesses should be investigated in line with a psychobiological approach, taking into account the interaction of different potentially causal determinants.

A noteworthy finding was the very high rates of alternative therapy consultations in the sensitive groups, especially IEI-EMF, in agreement with some evidence in the literature [80] and [81]. Solutions might be sought in better communication between patients and physicians. Dealing with medically unexplained conditions is an

important and challenging task for primary care that requires time and serious consideration of patient's concerns and at the same time prevention of unnecessary interventions [82] and [83]. Medical training does not prepare physicians to deal with symptomatic conditions such as IEI-EMF. As a result, their advice and recommendations are often not evidence-based, leading patients to further insecurity [84]. There is a need for the development and dissemination of a multidisciplinary case-definition protocol, which will constitute a first step towards the identification of environmental sensitivities in primary care and the development of effective treatment strategies.

COMPETING INTEREST STATEMENT

The authors have no competing interests to report.

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TABLES

Table 1. : Basic demographic characteristics, morbidity and lifestyle indicators of the three investigated groups (valid cases)

	NS group (n = 5073)	GES group (n = 514)	IEI-EMF group (n = 202)
<i>Demographic characteristics</i>			
Age (%)			
18–24	6.4	3.3 ^a	3.0
25–44	32.2	23.0 ^a	20.8 ^b
45–64	39.8	42.8	39.6
65–74	12.3	16.1 ^a	14.8
75 +	9.3	14.8 ^{and}	21.8 ^{and}
Mean age (SD)	51.0 (17.0)	56.5 (16.5) ^a	58.5 (17.7) ^b
Female gender (%)	56.0	78.0 ^{and}	61.4 ^c
Education (%) ^d			
Lower	22.4	27.0 ^a	34.2 ^b
Middle	44.8	45.2	41.3
Higher	32.8	27.8 ^a	24.5 ^b
Marital status (%)			
Unmarried	20.2	19.0	23.6
Married, living together	64.8	60.0 ^a	57.8 ^b
Divorced	7.0	12.4 ^a	7.5
Widowed	8.0	8.6	11.1
Occupational status (%)			
Employed, school, housewife/man	73.5	62.5 ^a	62.9 ^b
Unemployed, incapacitated	7.8	13.0 ^a	10.4
Retired	18.7	24.5 ^a	26.7 ^b
Born in the Netherlands (%)	93.8	89.8 ^a	84.4 ^b

	NS group (n = 5073)	GES group (n = 514)	IEI-EMF group (n = 202)
<i>Medical morbidity (registered) (%)</i>			
Asthma	3.5	5.4 ^a	4.5
Acute myocardial infarction	.9	.4	2.5 ^{and}
Chronic obstructive pulmonary disease (COPD)	2.6	4.7 ^a	3.0
Diabetes	5.7	8.4 ^a	8.9
Duodenal/peptic ulcers	.2	.0	.6
Hypertension (uncomplicated)	12.0	15.4 ^a	14.9
Rheumatoid arthritis	.6	1.2	.5
Herpes zoster	.5	1.4 ^a	.5
Psoriasis	.9	.6	2.5 ^{and}
Cancer (malignant neoplasm)	2.6	5.1 ^a	3.5
<i>Psychiatric morbidity (registered) (%)</i>			
Anxiety disorder	1.0	3.1 ^a	1.0
Depressive disorder	2.3	4.5 ^a	3.0
<i>Lifestyle indicators</i>			
Mean BMI (body mass index) (SD)	25.4 (4.8)	25.4 (5.1)	26.0 (4.6)
Smoking (%)			
No, never	42.7	43.3	46.5
No, in the past	36.8	40.5	34.5
Yes	20.5	16.2 ^a	19.0
Alcohol and/or substance abuse > 6 months (%)	1.8	3.0	2.3

Note: Significance level set at $p < .05$.

^A Significant difference between GES & NS group.

^B Significant difference between IEI-EMF & NS group.

^C Significant difference between GES & IEI-EMF group.

^D Lower: No education or primary school or lower secondary education; Middle: Intermediate vocational or intermediate general secondary or higher general secondary education; Higher: Higher vocational or university education.

Table 2. Prevalence of 23 self-reported NSPS in the NS, GES & IEI-EMF group and between-group differences^a

Self-reported NSPS	Corresponding ICPD code(s)	NS ^b	GES ^c	OR (95% CI)	IEI-EMF	OR (95% CI)
Fatigue/tiredness	A04	52.4	68.5	1.8 (1.5–2.3)*	62.2	1.5 (1.1–2.1) [†]
Abdominal/stomach pain	D01–D02, D06	22.8	39.9	2.0 (1.6–2.5)*	30.2	1.5 (1.1–2.2) [†]
Nausea	D09	11.2	20.8	1.8 (1.4–2.4)*	15.3	1.4 (.9–2.3)
Diarrhea or constipation	D11–D12	20.4	31.5	1.7 (1.3–2.1)*	23.0	1.1 (.8–1.7)
Eye symptoms	F01–F02	17.8	31.4	1.8 (1.4–2.3)*	23.8	1.3 (.9–1.9)
Ear symptoms	H01–H03, H13	12.7	21.3	1.6 (1.2–2.1)*	20.9	1.6 (1.0–2.3) [†]
Heart palpitations/awareness	K04	12.6	21.7	1.5 (1.2–1.9) [†]	26.3	2.3 (1.6–3.4)*
Neck or shoulder symptoms	L01, L08	37.0	54.3	1.7 (1.4–2.1)*	47.2	1.4 (1.0–2.0) [†]
Back pain	L02–L03	34.9	49.2	1.6 (1.3–2.0)*	42.7	1.3 (.9–1.8)
Pain/pressure in chest and heart region	L04, K01–K03	8.6	16.4	1.9 (1.4–2.5)*	20.0	2.5 (1.6–3.8)*
Arm/elbow/hand/wrist symptoms	L09–L12	23.7	37.3	1.5 (1.2–1.9)*	27.8	.9 (.6–1.4)
Leg/hip/knee/foot symptoms	L13–L15, L17	31.6	46.3	1.4 (1.2–1.8)*	42.4	1.2 (.8–1.7)
Pain in muscles	L18	30.3	41.2	1.5 (1.2–1.9)*	38.5	1.5 (1.0–2.1) [†]
Headache	N01–N02	36.8	51.0	1.8 (1.5–2.2)*	43.6	1.7 (1.2–2.5) [†]
Tingling of fingers, feet or	N05	15.7	27.0	1.6 (1.3–	25.0	1.6 (1.1–

Self-reported NSPS	Corresponding ICPC code(s)	NS ^b	GES ^c	OR (95% CI)	IEI-EMF	OR (95% CI)
toes				2.0)*		2.3)†
Dizziness or feeling light-headed	N17	19.4	37.4	2.0 (1.6–2.5)*	36.5	2.3 (1.7–3.3)*
Sleep problems	P06	25.6	42.7	1.7 (1.4–2.1)*	44.4	2.2 (1.5–3.0)*
Memory or concentration problems	P20	19.8	36.2	2.0 (1.6–2.4)*	35.0	1.9 (1.4–2.8)*
Shortness of breath	R02–R04, R29	7.8	17.0	2.0 (1.5–2.6)*	16.3	1.9 (1.2–3.0)‡
Cough	R05	21.9	27.2	1.2 (.99–1.5)	27.8	1.4 (1.0–2.1)†
Nasal symptoms	R07	24.5	37.8	1.8 (1.5–2.2)*	26.0	1.1 (.8–1.6)
Skin symptoms	S01, S06–S07	21.8	38.2	2.1 (1.7–2.6)*	35.6	1.9 (1.4–2.7)*
Weight change	T07–T08	11.6	16.9	1.3 (.99–1.7)**	18.5	1.7 (1.1–2.6)†

Note: †p < .05; ‡p < .01; *p < .001; **p = .05.

Abbreviations: OR, Odds ratio; CI, Confidence interval.

^A Between-group differences were adjusted for age, gender, education, ethnic background, medical morbidity, psychiatric morbidity.

^B Reference group.

^C No significant differences between GES & IEI-EMF group.

Table 3. Prevalence of self-reported NSPS with duration of ≥ 4 months in the NS, GES & IEI-EMF group and between-group differences^a

Self-reported NSPS	NS ^b	GES ^c	OR (95% CI)	IEI-EMF	OR (95% CI)
Fatigue/tiredness	23.3	42.5	2.0 (1.6–2.5)*	34.6	1.6 (1.1–2.3)‡
Abdominal/stomach pain	8.7	20.9	2.4 (1.8–3.1)*	14.0	1.5 (.9–2.4)
Nausea	2.2	8.2	2.7 (1.8–4.1)*	3.4	1.1 (.4–2.8)
Diarrhea or constipation	6.2	14.1	2.0 (1.5–2.7)*	10.1	1.4 (.8–2.5)

Self-reported NSPS	NS ^b	GES ^c	OR (95% CI)	IEI-EMF	OR (95% CI)
Eye symptoms	6.4	14.6	2.0 (1.5–2.8)*	10.7	1.3 (.7–2.2)
Ear symptoms	6.4	11.6	1.6 (1.1–2.2)†	13.2	1.7 (1.0–2.8)‡
Heart palpitations/awareness	5.6	11.2	1.6 (1.2–2.3)†	15.1	2.8 (1.8–4.5)*
Neck or shoulder symptoms	19.3	34.0	1.7 (1.4–2.2)*	24.0	1.1 (.7–1.6)
Back pain	18.3	32.1	1.7 (1.4–2.2)*	25.4	1.3 (.9–1.9)
Pain/pressure in chest and heart region	3.4	8.8	2.4 (1.6–3.5)*	8.3	2.4 (1.3–4.5)†
Arm/elbow/hand/wrist symptoms	13.7	25.5	1.6 (1.2–2.0)*	17.6	1.0 (.6–1.6)
Leg/hip/knee/foot symptoms	19.5	32.8	1.5 (1.2–1.8)†	26.6	1.0 (.7–1.5)
Pain in muscles	8.5	18.4	1.9 (1.4–2.5)*	19.4	2.0 (1.3–3.0)†
Headache	10.2	24.5	2.6 (2.0–3.3)*	16.6	2.0 (1.3–3.0)†
Tingling of fingers, feet or toes	8.6	16.7	1.7 (1.2–2.2)*	12.7	1.3 (.8–2.1)
Dizziness or feeling light-headed	7.2	19.1	2.4 (1.8–3.2)*	16.0	2.2 (1.4–3.5)*
Sleep problems	14.6	29.9	1.9 (1.5–2.4)*	28.2	2.1 (1.4–3.0)*
Memory or concentration problems	11.4	26.3	2.3 (1.8–2.9)*	20.7	1.8 (1.2–2.8)†
Shortness of breath	4.1	10.1	2.3 (1.6–3.2)*	7.5	1.6 (.8–3.0)
Cough	5.3	8.0	1.3 (.9–2.0)	11.8	2.1 (1.2–3.5)†
Nasal symptoms	10.3	19.7	2.0 (1.5–2.6)*	12.6	1.1 (.7–1.9)
Skin symptoms	11.7	25.7	2.4 (1.9–3.0)*	18.0	1.4 (.9–2.2)
Weight change	6.4	11.6	1.6 (1.2–2.2)†	9.4	1.4 (.8–2.5)

Note: †p < .05; ‡p < .01; *p < .001; **p = .05.

Abbreviations: OR, Odds ratio; CI, Confidence interval.

^A Between-group differences were adjusted for age, gender, education, ethnic background, medical morbidity, psychiatric morbidity.

^B Reference group.

^C Significant differences between GES & IEI-EMF (ref) group: abdominal/stomach pain (OR 1.7, 95% CI 1.0–3.0, p<.05), nausea (OR 2.7, 95% CI 1.0–7.4, p<.05), neck or shoulder symptoms (OR 1.6, 95% CI 1.0–2.4, p<.05), nasal symptoms (OR 1.8, 95% CI 1.1–3.2, p<.05).

Table 4. Unadjusted and adjusted differences between groups on determinants of functional status, illness behavior, symptom perceptions & symptom scores

	GES vs. NS ^a		IEI-EMF vs. NS ^a		GES vs. IEI-EMF ^a	
	Unadjusted	Adjusted ^b	Unadjusted	Adjusted ^b	Unadjusted	Adjusted ^b
<i>Regression coefficient (95% CI)</i>						
General health	- 9.1 (- 11.0 to - 7.4)*	- 7.4 (- 9.0 to - 5.7)*	- 6.6 (- 9.3 to - 3.9)*	- 3.9 (- 6.5 to - 1.2)†	- 2.5 (- 6.1 to 1.0)	- 3.1 (- 6.7 to .5)
Sleep quality	.9 (.7 to 1.2)*	.6 (.4 to .9)*	1.0 (.6 to 1.4)*	.9 (.5 to 1.3)*	-.07 (- .6 to .4)	-.2 (- .8 to .3)
Psychological distress	1.3 (.8 to 1.8)*	1.0 (.5 to 1.5)*	.9 (.2 to 1.7)†	1.0 (.2 to 1.8)†	.3 (- .6 to 1.4)	.04 (- 1.0 to 1.1)
Perceived impact ^c	1.2 (.9 to 1.4)†	1.0 (0.7 to 1.2)*	.6 (.2 to 1.1)†	.5 (.09 to 1.0)†	.5 (.02 to 1.0)†	.4 (- .05 to 1.0)
Emotional response ^c	1.5 (1.2 to 1.8)*	1.3 (1.0 to 1.6)*	.8 (.3 to 1.3)†	.8 (.3 to 1.4)†	.7 (.1 to 1.2)†	.6 (- .01 to 1.2)**
Number of self-reported NSPS	2.6 (2.3 to 3.0)*	2.1 (1.8 to 2.5)*	1.8 (1.2 to 2.4)*	1.7 (1.1 to 2.3)*	.8 (.03 to 1.6)†	.5 (- .3 to 1.3)
Duration of self-reported NSPS	9.0 (7.8 to 10.1)*	7.2 (6.1 to 8.4)*	5.7 (3.8 to 7.5)*	5.0 (3.0 to 6.8)*	3.3 (.4 to 6.2)†	2.7 (- .3 to 5.7)
<i>OR (95% CI)</i>						
Consulting a GP	1.7 (1.3–2.2)*	1.2 (.98–1.6)	1.2 (.8–1.7)	1.0 (.7–1.5)	1.4 (.96–2.1)	1.2 (.8–1.9)
Consulting a psychologist	1.9 (1.5–2.4)*	1.9 (1.5–2.5)*	1.5 (1.0–2.3)†	2.0 (1.3–3.1)†	1.2 (.8–2.0)	1.0 (.6–1.6)
Consulting an alternative therapist	2.1 (1.6–2.7)*	1.9 (1.4–2.5)*	3.0 (2.0–4.4)*	3.8 (2.5–5.7)*	.7 (.4–1.0)	.5 (.3–.8)†
Unprescribed medication	1.3 (1.1–1.6)†	1.3 (1.1–1.6)†	1.0 (.7–1.3)	1.1 (.8–1.6)	1.3 (.97–1.9)	1.2 (.8–1.8)
Registered NSPS	1.3 (1.1–1.6)†	1.1 (.9–1.4)	1.3 (.99–1.7)	1.0 (.7–1.4)	1.0 (.7–1.4)	1.1 (.7–1.6)
Prescribed painkillers	1.4 (1.1–1.7)†	1.2 (.97–1.5)	1.4 (1.0–2.0)†	1.2 (.9–1.8)	1.0 (.7–1.4)	.9 (.6–1.4)
Prescribed benzodiazepines	2.1 (1.6–2.7)*	1.4 (1.0–1.8)†	1.9 (1.3–2.8)†	1.5 (1.0–2.4)**	1.1 (.7–1.7)	1.0 (.6–1.6)

	GES vs. NS ^a		IEI-EMF vs. NS ^a		GES vs. IEI-EMF ^a	
	Unadjusted	Adjusted ^b	Unadjusted	Adjusted ^b	Unadjusted	Adjusted ^b
Prescribed antidepressants	2.2 (1.7–2.9)*	1.5 (1.1–2.1)†	1.5 (.95–2.4)	1.3 (.7–2.3)	1.5 (.9–2.4)	1.1 (.6–2.0)

Note: †p < .05; ‡p < .01; *p < .001; **p = .05.

Abbreviations: OR, Odds ratio; CI, Confidence interval.

A Reference group.

B Between-group differences were adjusted for age, gender, education, ethnic background, medical (co)morbidity, psychiatric (co)morbidity.

C Referring to the most important symptom among the ones reported.

Table 6. Association between number and duration of self-reported NSPS and prevalence of illness behavior & symptom perceptions in the three examined groups†

Illness behavior & symptom perceptions	Number of symptoms				Duration of symptoms			
	0–1	2–9	10–14	≥ 15	< 50th percentile	50th–79th percentile	80th–94th percentile	95th percentile
<i>Consulting a GP</i>								
NS ^{and} (V _{number} = .22, V _{dur.} = .23) ^c	55.0	74.7	88.7	91.5	62.8	79.4	86.6	89.3
GES ^{and} (V _{number} = .15, V _{dur.} = .21) ^c	74.1	78.4	90.4	90.0	71.8	77.6	90.4	90.6
IEI-EMF ^b (OR _{number} = 1.38, V _{dur.} = .23) ^c	76.0‡		81.4‡		64.5	81.6	84.6	88.0
<i>Consulting a psychologist</i>								
NS ^{and} (V _{number} = .19, V _{dur.} = .18) ^c	4.5	9.1	21.8	33.3	5.6	11.3	16.4	27.0
GES ^{and} (V _{number} = .18, V _{dur.} = .2) ^c	3.8	14.4	27.8	24.4	7.8	15.8	22.6	29.4
IEI-EMF ^{and} (OR _{number} = 4.2, V _{dur.} = .33)	9.7‡		31.0‡		6.8	5.4	23.1	37.5
<i>Consulting an alternative therapist</i>								
NS ^{and} (V _{number} = .1, V _{dur.} = .14) ^c	3.7	7.6	12.7	16.5	4.3	9.3	13.0	14.5
GES ^{and} (V _{number} = .15, V _{dur.} = .15) ^c	3.8	12.9	20.9	26.8	8.7	12.9	23.3	16.5
IEI-EMF (OR _{number} = 1.99, V _{dur.} = .16) ^c	17.9‡		30.2‡		15.5	26.3	17.9	33.3
<i>Unprescribed medication</i>								

Illness behavior & symptom perceptions	Number of symptoms				Duration of symptoms			
	0-1	2-9	10-14	≥ 15	< 50th percentile	50th-79th percentile	80th-94th percentile	95th percentile
NS ^{and} (V _{number} = .22, V _{dur.} = .16) ^c	27.4	53.7	61.6	66.9	41.9	57.5	58.4	62.4
GES (V _{number} = .05, V _{dur.} = .08) ^c	50.0	57.6	60.2	60.0	52.3	58.1	62.7	61.2
IEI-EMF ^a (V _{number} = .23, V _{dur.} = .17) ^c	26.7	50.0	68.8	36.4	41.1	52.8	62.2	58.3
<i>Consequences</i> [†]								
NS ^{and} (r _{number} = .36, r _{dur.} = .42) ^c	4.3 (2.7)	5.3 (2.6)	7.1 (2.1)	7.9 (1.7)	4.4 (2.6)	5.6 (2.4)	6.7 (2.2)	8.0 (1.8)
GES ^{and} (r _{number} = .39, r _{dur.} = .44) ^c	5.0 (3.1)	6.2 (2.5)	7.6 (1.9)	8.0 (2.0)	5.0 (2.6)	6.2 (2.4)	7.1 (2.1)	8.2 (1.6)
IEI-EMF ^{and} (r _{number} = .36, r _{dur.} = .47) ^c	6.7 (.9)	5.7 (2.6)	7.6 (2.1)	7.5 (2.6)	5.4 (2.5)	4.9 (2.6)	7.2 (1.8)	8.2 (1.7)
<i>Emotional response</i> [†]								
NS ^{and} (r _{number} = .36, r _{dur.} = .37) ^c	2.8 (2.9)	4.0 (2.9)	6.0 (2.7)	7.0 (2.4)	3.1 (2.8)	4.2 (2.9)	5.6 (2.8)	6.7 (2.7)
GES ^{and} (r _{number} = .33, r _{dur.} = .37) ^c	5.5 (2.1)	5.3 (2.8)	6.1 (2.9)	7.8 (2.2)	4.3 (2.8)	5.2 (2.7)	6.2 (2.7)	7.3 (2.6)
IEI-EMF ^{and} (r _{number} = .32, r _{dur.} = .37) ^c	5.0 (3.8)	4.7 (3.0)	6.2 (2.7)	8.0 (1.8)	4.3 (3.0)	4.6 (3.0)	5.6 (3.1)	7.4 (2.2)

†Data per symptom category are given as percentage of participants, except for “Perceived impact” & “Emotional response” which are given as mean scores and their standard deviations (SD). Note: Significance level set at $p < .05$.

‡IEI-EMF group: When the expected count in the chi-squared test was < 5 in more than one cell (symptom category), the symptom number & duration scores were dichotomized (cut-off point: ≤ 10 symptoms & ≤ 80 th percentile respectively).

†Referring to the most important symptom among the ones reported.

^A Significant difference between symptom number categories across rows.

^B Significant difference between symptom duration categories across rows.

^C Effect sizes representing the strength of associations between indicators of illness behavior and symptom perceptions and symptom number and duration for each group; for the associations with the continuous indicators the original symptom sum scores were used (abbreviations: r, Pearson r coefficient; V, Cramer's V; OR, Odds ratio).