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Neighbourhood social and physical environment and general practitioner assessed morbidity



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ABSTRACT

The aim of our study was to investigate the association between health enhancing and threatening, and social and physical aspects of the neighbourhood environment and general practitioner (GP) assessed morbidity of the people living there, in order to find out whether the effects of environmental characteristics add up or modify each other. We combined GP electronic health records with environmental data on neighbourhoods in the Netherlands. Cross-classified logistic multilevel models show the importance of taking into account several environmental characteristics and confounders, as social capital effects on the prevalence of morbidity disappear when other area characteristics are taken into account. Stratification by area socio-economic status, shows that the association between environmental characteristics and the prevalence of morbidity is stronger for people living in low SES areas. In low SES areas, green space seems to alleviate effects of air pollution on the prevalence of high blood pressure and diabetes, while the effects of green space and social capital reinforce each other.

1. Introduction

Chronic illness and medically unexplained physical symptoms are highly prevalent and have high impact on quality of life and associated high costs (Murray et al., 2016). Traditionally, the emphasis has been on individual determinants. However, during the past decades the focus shifted towards environmental characteristics and their interaction with individual characteristics (MacIntyre and Ellaway, 2000; Sallis et al., 2008). Exposure to environmental influences occurs in several contexts, of which the direct environment of the residential neighbourhood is the most important. In this article we focus on neighbourhood influences on health. There are still many knowledge gaps about the relationships between neighbourhood characteristics and health. We will address three of them.

First of all, although it is common knowledge that different dimensions of the neighbourhood environment have an influence on health, analyses often have only addressed one specific dimension (examples: for green space De Jong et al., 2012; for social safety: Lovasi et al., 2014; for social capital: Giordano et al., 2011; for air quality: Jacquemin et al., 2015). Consequently, there is a gap in our knowledge on the relative contribution of different aspects of the environment and their interplay in affecting health (Ruijsbroek et al., 2016).

Secondly, it is important to address potential confounding variables at the neighbourhood level and not only at individual level. We will therefore take into account the socio-economic status of neighbourhoods, ethnic population composition and urbanicity. These characteristics may be in a complex relation with the environmental characteristics that we will study, partly influencing environmental characteristics and partly interacting with them in influencing health.

A final issue is related to the emphasis on either health threatening or enhancing aspects of the environment. Particulate matter in the air and ticks in the local park are health threatening, while nice and well-

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	Physical environment	Social environment
Health enhancing	Green space	Social capital
Health threatening	Air pollution	Neighbourhood unsafety

Fig. 1. Matrix of two dimensions of the neighbourhood environment with examples of characteristics in each combination.

kept street greenery is health enhancing. The same holds for social capital that is considered as health benefit, while low neighbourhood safety is a health threat. These examples show that health threatening and enhancing are not just opposite poles of the same dimension, but are qualitatively different and might have their own and combined effects on health. Over time, there is an increasing attention for health enhancing or salutogenic environments (Lindström and Eriksson, 2005). In our study we will address these knowledge gaps by studying health threatening and health enhancing influences of characteristics of both social and physical environments, including their interrelationships. Although there is not a strict distinction between physical and social environment, as we live in a largely man-made world, the physical environment refers to spatial characteristics and physical exposures, while the social environment is usually understood to refer to characteristics based on social activities and life style (see for example the conceptual framework of Schulz et al., 2005). This results in the matrix in Fig. 1. The cells of the matrix contain the influences that we will study in this article.

An important question is how these different influences relate to each other in their net effect on health. The most straightforward argument is that they have separate, additive effects on health. It is however also conceivable that health enhancing features of the neighbourhood environment alleviate the negative effects of health threats. Effects of air pollution, for example, might be weakened by social capital and green space. Furthermore, positive or negative features can reinforce each other. For example, social capital effects might become stronger if there are also green spaces in a neighbourhood, or the health consequences of air pollution might be worse in neighbourhoods that are unsafe. Finally, there might be a difference in strength in effects regarding physical and social environmental conditions: Green spaces might be more important than social capital.

Studies on the relationship between neighbourhood characteristics and health use a wide variety of outcome measures. They can be divided into self-reports and physician-assessed measures and into general and physical/somatic health measures and mental health. The most commonly used health variable is self-reported health. Apart from that, mortality, either or not by cause, has been used (Gascon et al., 2016) and the prevalence of specific diseases, such as depression (Zijlema et al., 2016), or a broader range of clusters of disease as assessed by general practitioners (GPs) (Maas et al., 2009).

Our study is largely explorative in its use of a wide range of health outcomes. We will use GP-assessed morbidity and we will select a number of clusters of morbidity, based on systematic reviews, highlighting the most common pathways between neighbourhood characteristics and health. Some of these pathways are specific to certain kinds of exposure in the neighbourhood, whilst others are rather generic.

One of the clusters is cardiovascular diseases which are often seen as influenced by environmental stress (Kim et al., 2008). Exposure to particulate matter is related to cardiovascular disease through physical mechanisms (Brook et al., 2010). A review concluded that there is evidence of reduced cardiovascular disease mortality with more green space in the residential environment (Gascon et al., 2016).

Both social and physical characteristics of neighbourhoods are related to increased stress and less social contacts. Through these pathways they may be related to mental and neurological disorders and so-called medically unexplained physical symptoms (MUPS, e.g. weakness/tiredness, abdominal pain, headache, back complaints) (Hartig

et al., 2014; Lorenc et al., 2012; Ehsan and De Silva, 2015). MUPS are highly prevalent in the general population (Van der Windt et al., 2008) and related to (perceived) environmental threats (Spurgeon, 2002; Baliatsas et al., 2011).

Different gaseous and particulate air pollutants have been related to respiratory morbidity and mortality. Most evidence points to an increased risk of exacerbations. The onset of COPD (due to accelerated pulmonary function decline) and the incidence of asthma have been linked to air pollution (Kurt et al., 2016; Jacquemin et al., 2015).

Recently, a relation was established between diabetes and air pollution (Eze et al., 2015). In view of the expected increase of the prevalence of type 2-diabetes, this is an important finding, which is still in need of further replication. The evidence for the Netherlands is small and still inconclusive (Dijkema et al., 2011).

Against this background, we will answer the following research questions:

How are social and physical aspects of the neighbourhood environment, conceived as health enhancing and health threatening, related to morbidity of the people living there?

Are these different environmental characteristics additive in their effects on morbidity or do they modify each other's effects?

2. Data, measurements and methods

2.1. Data

The main source of our data was the NIVEL Primary Care Database (Prins et al., 2015; https://www.nivel.nl/en/dossier/nivel-primarycare-database). This database holds data extracted from the electronic health records systems, kept routinely as part of the care process by general practitioners (GPs). As nearly all Dutch are registered with a specific GP or practice, morbidity data from general practice give a good overview of the health of the population (Westert and Jabaaij, 2006). GPs record the information on symptoms and diagnoses using the International Classification of Primary Care (ICPC) (Lamberts and Wood, 1987). Patient records of different consultations were combined into disease episodes. Data from one calendar year (2013) were used in order to avoid seasonal influences/differences. Patients who consulted their GP for chronic illnesses in 2011 and 2012 were regarded as chronically ill in 2013 as well, even if they had not consulted their GP for this illness in 2013. The data refer to 1,16 million people of all ages (7% of the Dutch population), registered with 347 practices, who were with the same practice during all 12 months of 2013. As individual level socio-demographic characteristics, the database only contains age and sex.

Data sources for the other independent variables will be described in the next section.

2.2. Measurements

2.2.1. Dependent variables

As an indicator for health, we used the morbidity as presented to GPs during one-year.

Health problems were grouped into ten clusters of ICPC, following Maas et al. (2009). Diagnoses were combined with related symptoms in order to decrease variation across GPs in recording practices. Not all clusters were mutually exclusive. We selected four clusters of cardio-vascular morbidity: (1) high blood pressure, (2) cardiac disease, (3) coronary heart disease, and (4) stroke and brain hemorrhage. With respect to mental health problems we selected two clusters: (5) depression and (6) anxiety disorder. In neurological disorders we selected (7) migraine/severe headache. From respiratory disorders we selected (8) asthma and Chronic Obstructive Pulmonary Disease (COPD). Various symptoms were combined into the cluster (9) Medically Unexplained Physical Symptoms (MUPS). Finally we selected (10) diabetes. The dependent variable is the binary variable

whether or not someone had at least one disease episode in a cluster.

2.2.2. Independent variables at the area level

As area level we used four digit postal code areas (see Section 2.3).

2.2.2.1. Green space. Information on green space was derived from the National Land Use database (LGN7) for 2012. LGN-7 contains the dominant type of land use of each $25 \times 25 \,\mathrm{m}$ grid cell in the Netherlands (Hazeu, 2014). We used total green space (agricultural green, woods and nature areas), expressed as % of total number of grid cells in each postal code area.

2.2.2.2. Air pollution. Exposure to air pollution was estimated by land use regression models in the framework of the ESCAPE study (Eeftens et al., 2012). The models were developed based upon measurements in 2009 and predictors such as traffic flow, population density and land use obtained from geographic information systems. The models have been applied to all addresses in the Netherlands. The 95-percentile of the distribution of modelled levels at living addresses was used to assess the aggregated neighbourhood level. The following indicators were used: PM_{10} in $\mu g/m^3$, $PM_{2.5}$ in $\mu g/m^3$ and NO_2 in $\mu g/m^3$. We used the 95th percentile instead of the mean to characterize the air pollution level, to give more weight to highly polluted locations such as major roads. 95th percentile and mean were highly correlated for all pollutants. Consistently, associations with health were similar for the two metrics in initial analyses.

2.2.2.3. Social capital. A measure of social capital was constructed on the basis of the 'Housing and Living Survey' made available by Statistics Netherlands. This survey investigates the housing situation of people in the Netherlands and contains information on contacts within the neighbourhood and on individual-level characteristics (Ministerie van Binnenlandse Zaken en Koninkrijksrelaties, 2012). Data were collected from 69,336 people between September 2011 and May 2012 (response rate 58%). Statistics Netherlands gave access to data of postal code areas with at least three respondents, resulting in 2544 areas with on average 27 respondents. Data were collected by telephone, face-to-face interviews and Internet. Participants were randomly selected from the population of Dutch households with at least one person aged 18 years or above. The area social capital measure was constructed, using an ecometric analysis (Raudenbush, 2003), from five questions on contacts with direct neighbours; contact with other neighbours; whether people in the neighbourhood know each other; whether neighbours are friendly to each other; and whether there is a friendly and sociable atmosphere in the neighbourhood. Response categories were 'totally agree', 'agree', 'neutral', 'don't agree', and 'totally don't agree' (coded 1-5). The area social capital measure was created through three-level multilevel regression analysis of the 5 items adjusted for background characteristics of the respondents to take into account variations in the sampled respondents (following Mohnen et al. (2011) and Waverijn et al. (2016)). Higher values indicate more social capital. Reliability of the social capital measure (Raudenbush, 2003) at postal code area level was 0.74, indicating a satisfactory reliability.

2.2.2.4. Neighbourhood unsafety. Neighbourhood unsafety was measured by the frequency of crime people perceived to happen in their neighbourhood and feelings of unsafety. These measures were derived from the Dutch Integral Safety Monitor 2011 (Integrale Veiligheidsmonitor), conducted by Statistics Netherlands (CBS). This is a nationwide survey of non-institutionalized persons aged 15 years and older. Data were collected via Internet or a mailed questionnaire.

Non-responders were approached again by telephone or face-to-face. A total of 223,944 respondents completed the survey in 2011 (response rate 43%). We selected respondents of 18 years and older (N = 216,840). Statistics Netherlands gave access to data of postal code areas with at least four respondents, resulting in 2626 areas with on average 73 respondents.

A perceived area level crime frequency score was created through three-level multilevel regression (ecometric) analysis of the answers of respondents to five questions concerning the frequency of specific crime events in their neighbourhood: bicycle theft, theft from cars, threats, burglary and muggings. Possible answers were 'often', 'sometimes' and '(almost)never'. Unsafety feelings were measured by the question: 'Do you ever feel unsafe in your neighbourhood?' (answers: 'yes', 'no') (Ruijsbroek et al., 2015) and the corresponding variable was constructed through a two-level multilevel regression analysis. Both variables were adjusted for background characteristics of the respondents

2.2.3. Confounding variables at the area level

2.2.3.1. Ethnic composition. This variable was provided by Statistics Netherlands for 2013. It is based on the country of birth of parents and grandparents. If one of the parents or grandparents was born outside the Netherlands, the person is classified as immigrant. The variable used is the percentage of non-Western immigrants per area. Immigrant status at individual level was not available; hence, this area variable is partly a proxy for unmeasured individual immigrant status.

2.2.3.2. Area Socio-Economic Status. Area Socio-Economic Status (SES) was developed by the Netherlands Institute for Social Research and available from Statistics Netherlands for 2014. It is based on average income, the percentage of people with a low income, the percentage of people with low education and the percentage of non-working people. Via factor analysis these were combined to form one variable (Knol et al., 2012). As we don't have the equivalent individual variables, area SES is also partly a proxy for unmeasured individual socio-economic status.

2.2.3.3. Urbanity. This variable was obtained from Statistics Netherlands for 2013. At the level of the postal code areas, the density of inhabitants was used. At municipal level, we added the commonly used five categories ranging from very strongly urban (1) to non-urban (5), based on the number of households per square km, which is widely used in the Netherlands (Den Dulk et al., 1992)

2.2.4. Confounders at individual level

At individual level we could only include age and sex of all people registered with the GP practices. Other confounders, such as socioeconomic status, were not available.

2.3. Spatial scale

We see neighbourhoods as the direct living environment of people where part of their activities takes place, where they create community (Volker et al., 2007), and where they are exposed to positive and negative environmental influences. However, the different environmental influences that we study, might require a definition of neighbourhoods at different spatial scales. For example, for the effect of exposure to air pollution a very small spatial scale is appropriate, while the effect of green space through physical activity might need a larger scale. Availability of data has largely determined our choice of four-

digit postal code areas in the Netherlands. Their surface varies between 1 and $8\,\mathrm{km}^2$, with an average population of 4160 (interquartile range 6140). In urban areas, they are relatively small, with a higher number of inhabitants and consequently denser population; in urban, areas postal code areas largely coincide with urban neighbourhoods. In rural areas, there is more diversity with whole villages or settlements and the surrounding area belonging to the same postal code area.

The total number of postal code areas in the Netherlands was 4033. As we used data from different sources, including surveys, complete data were available for 2070 postal code areas, both rural and urban, nested in 390 municipalities (see Additional Fig. A1).

2.4. Statistical analysis

2.4.1. Nested structure of the data

We use multilevel analysis to analyse the data (Snijders and Bosker, 2012). We distinguish four levels. At the lowest level, we use cells, formed by the combination of six age categories (0–4, 5–12, 13–18, 19–39, 40–64, 65 years and older) and sex, with the number of people having at least one episode in the disease cluster as numerator and the number of people in the cell as the denominator. The proportion in each cell is the outcome variable. This approach was chosen because of the large number of patients in this study (Goldstein, 2010; for an application see Turrell et al. (2007)). Cells are nested in GP practices and in postal code areas within municipalities, but these are not hierarchical; GPs may have patients in different postal code areas and people in the same postal code area may be registered with different GP practices. Postal code areas are nested within municipalities. Fig. 2 contains a diagram of the data structure. For ease of formulation, we use the term patients to denote the lowest level.

2.4.2. Statistical model

Multilevel analysis uses empirical Bayes estimates to take into account for different numbers of observations within the higher-level units (Diez Roux, 2002). Because of the incomplete hierarchy we used cross-classified models (Goldstein, 2010) of cells nested both in GP practices and postal code areas; the postal code areas are moreover nested within municipalities. Because of the nature of the dependent variables, proportions, we used multilevel regression with the binomial logit link (estimation procedure first order PQL, software MLwiN 2.30).

2.4.3. Modelling strategy

We performed separate analyses for each of the ten morbidity

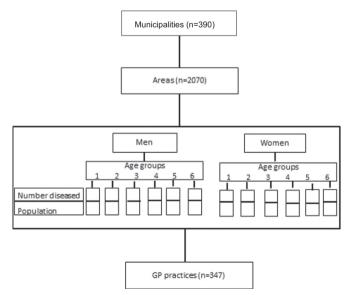


Fig. 2. Diagram of the multilevel data structure (after Turrell et al. (2007)).

Distribution of the independent variables at individual level, percentages (N = 1,159,929) and neighbourhood level, mean and interquartile range (IQR) (N = 2070), compared to the Dutch population.

Individual level	Study pop	ulation (%)	Dutch pop	ulation (%)
Women	50.7		50.5	
Men	49.3		49.5	
Age 0-4 years	5.1		5.4	
Age 5-12 years	9.8		9.3	
Age 13-18 years	7.2		7.1	
Age 19–39 years	25.6		25.8	
Age 40-64 years	36.1		35.5	
Age 65 years and older	16.2		16.8	
Neighbourhood level	Mean	IQR	Mean	IQR
Social capital	0.16	1.33	0.16	1.32
Feelings of unsafety	-1.6	0.54	-1.6	0.52
Perceived crime frequency	-0.51	1.03	-0.54	1.04
Percentage green space	39.6	71.6	41.0	72.9
PM ₁₀ in μg/m ³	25.9	2.1	25.8	2.1
$PM_{2.5}$ in $\mu g/m^3$	17.2	1.5	17.2	1.5
$NO_2 (\mu g/m^3)$	28.3	10.3	28.0	10.1
Population density	1423.1	1763.8	1367.8	1728.1
Area SES	-0.074	0.13	-0.005	0.13
Percentage immigrants	19.7	16.3	19.4	16.2

Table 2 Annual prevalence (2013) of disease episodes in the study population in 10 morbidity clusters: ICPC-codes, number of patients in the respective morbidity category and patients per 100 of the study population (N = 1,159,929).

ICPC-codes	Number of patients	%
K85 K86 K87	179,341	15.5
K71 K73 K74 K77 K78 K79 K80 K81 K82 K83 K84	69,833	6.0
K74 K75 K76	46,868	4.0
K89 K90	25,804	2.2
P03 P76	44,147	3.8
P01 P74	38,107	3.3
R91 R95 R96	130,122	11.2
N01 N02 N03 N89 N90 N92	49,376	4.3
A01 A04 D01 D08 D09 D12 D18 D21 D93 K01 K02 K04 L01 L02 L03 L08 L09 L14 L20 N01 N02 N17 P06 P20 R02 R21 T03 T07 T08	336,985	29.1
T88 T90	71,302	6.1
	K85 K86 K87 K71 K73 K74 K77 K78 K79 K80 K81 K82 K83 K84 K74 K75 K76 K89 K90 P03 P76 P01 P74 R91 R95 R96 N01 N02 N03 N89 N90 N92 A01 A04 D01 D08 D09 D12 D18 D21 D93 K01 K02 K04 L01 L02 L03 L08 L09 L14 L20 N01 N02 N17 P06 P20 R02 R21 T03 T07 T08	K85 K86 K87 179,341 K71 K73 K74 K77 K78 K79 69,833 K80 K81 K82 K83 K84 K74 K75 K76 46,868 K89 K90 25,804 P03 P76 44,147 P01 P74 38,107 R91 R95 R96 130,122 N01 N02 N03 N89 N90 N92 49,376 A01 A04 D01 D08 D09 D12 D18 D21 D93 K01 K02 K04 L01 L02 L03 L08 L09 L14 L20 N01 N02 N17 P06 P20 R02 R21 T03 T07 T08

clusters selected for this study. This is not to say that the morbidity clusters are independent; however, there is overlap between some of the clusters and a multi-response model would in this case pose computational problems. We will present the correlations between the prevalence of the clusters at the area level. We estimated the baseline models, only including patients' age and sex, to estimate clustering of morbidity in the cross-classification of GP practices, postal code areas and municipalities.

Subsequently we estimated three sets of models. First, we estimated the fixed effects of the independent variables of interest, separately for each single variable (e.g. the baseline model + social capital; M1 in Table 3). Secondly, we added the area level confounders (e.g. the baseline model + social capital + area level confounders; M2 in Table 3). This was repeated for each of the independent variables.

It turned out that area SES and the percentage of immigrants in an area strongly attenuate the effects of the variables of interest. Postal code areas with a high percentage of immigrants are concentrated in

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Table 3

Multilevel logistic regression analysis (cross-classification of area and GP practice), separate analysis for each group of area variables; M1: adjusted for age and gender, M2: adjusted for age, gender and area level confounders (area SES, percentage immigrants, population density, urbanity of municipality) (B-coefficients). N study population = 1,159,929.

Morbidity cluster	High blood pressure	Cardiac disease	Coronary heart disease	Stroke, brain hemorrage	Depression	Anxiety disorder	Asthma, COPD	Migraine/ severe headache	Medically Unexplained Physical Symptoms	Diabetes
Social capital:										
M1	-0.193**	-0.130	-0.211	-0.294**	-0.475**	-0.306**	-0151**	-0.271**	-0.227**	-0.854**
M2	-0.04	0.012	0.089	-0.010	-0.079	-0.141	0.048	0.121	0.032	-0.102
Feelings of unsafe	ety:									
M1	0.02	0.049	0.072	0.084	0.087**	0.040	0.026*	0.053	0.038**	0.127^{**}
M2	0.007	0.043	0.050	0.076	0.051^{*}	0.023	0.007	0.019	0.010	0.031
Perceived crime f	requency:									
M1	0.03**	0.018	0.039*	0.036	0.057**	0.018	0.039^{**}	0.063	0.042**	0.084**
M2	0.012	0.004	0.006	0.021	-0.003	-0.017	0.013	0.013	0.007	-0.038^{*}
Percentage green	space:									
M1	-0.0006*	-0.001	-0.001	-0.002**	-0.003**	-0.002**	-0.0013**	-0.0015**	-0.001***	-0.003**
M2	-0.0005	-0.0006	-0.000	-0.0009	-0.0014	-0.0016**	-0.0005	-0.0005	-0.0007**	-0.0004
PM_{10} in $\mu g/m^3$:										
M1	0.013	-0.002	-0.027	-0.022	0.007	0.010	-0.009	-0.014	0.002	0.032^{*}
M2	0.008	-0.005	-0.036	-0.023	-0.002	0.008	-0.011	-0.027°	-0.001	0.001
$PM_{2.5}$ in $\mu g/m^3$:										
M1	-0.011	-0.002	0.030	0.054	0.004	-0.007	-0.0006	-0.003	0.001	-0.015
M2	-0.011	-0.004	0.028	0.048	0.001	-0.005	0.003	0.005	0.004	0.002
NO_2 ($\mu g/m^3$):										
M1	-0.003	0.001	0.005	0.004	0.004	0.003	0.003*	0.007	-0.001	0.001
M2	-0.004	-0.002	0.001	-0.001	-0.002	-0.003	0.0002	0.004	-0.005**	-0.009**

^{*} p < 0.05.

cities, whilst areas with low SES can be found all over the country. We therefore decided to stratify the analysis by area SES in quintiles. This results in the third set of models. For each variable of interest we first estimated a stratified model including age and sex of the patients and the variables of interest one by one (M1 in Table 4 and Additional Tables A4–A13). We then ran a model with all the variables of interest at the same time and the other area level confounders (M2 in Table 4 and Additional Tables A4–A13).

Finally, we estimated models with interactions between the variables of interest. To reduce the number of possible interactions we looked at two types of effects: alleviating and reinforcing effects. Alleviating effects were tested by using the interactions between green space and air pollution and between social capital and feelings of unsafety. Reinforcing effects were tested using the interactions between green space and social capital and between air pollution and feelings of unsafety. Based on the results of the previous steps, the interactions were only tested in the highest and lowest quintile of area SES. These models include age and sex of the participants, the area level confounders, the main effects of the variables of interest and the interactions, specified above.

The total number of participants is large enough for these analyses (n = 1,16 million); the lowest and highest SES quintiles together contain nearly half of the patients; the independent variables are continuous; and the interactions are combinations of continuous variables.

3. Results

3.1. Description of the study population

For age and sex, the study population shows the same distribution as the Dutch population (Table 1). The neighbourhoods in this study are a good representation of all neighbourhoods in the Netherlands.

The correlations between the neighbourhood variables are in

Additional Table A1.

Table 2 shows the dependent variables, the morbidity clusters. The ICPC-codes are given, the number of people that suffer from the diseases and symptoms in each cluster and the number per 100 of the study population. The study population are all participants in the NIVEL Primary Care Database. The neighbourhood level correlations between the morbidity clusters are in Additional Table A2.

Morbidity as assessed by GPs is clustered in Dutch neighbourhoods. However, this clustering is not very strong and for nearly all groups of morbidity, clustering within GP practices is stronger. The largest neighbourhood variance is found for diabetes (see Additional Table A3).

3.2. Area characteristics and the prevalence of morbidity

Overall, we find more significant relationships with the social aspects of the environment (social capital, feelings of unsafety and perceived crime frequency) and green space than with the indicators for air pollution (Table 3, M1). After adding the area level confounders to the models with age, sex and the area level variable of interest, many of the significant relationships disappear.

All significant relationships of social capital and all but one for perceived crime frequency disappear. Relationships of feelings of unsafety remain significant after introducing the area level confounders for the prevalence of cardiac disease, coronary heart disease, stroke/brain hemorrhage and depression. Also many of the significant relationships of green space disappear, except for those with depression, anxiety and MUPS.

Some of the significant relationships of the air pollution variables are contrary to the expectation; this applies to the relationships between PM_{10} with migraine/ severe headache and coronary heart disease and for NO_2 with MUPS and with diabetes. Also the relationship between perceived crime frequency and diabetes is contrary to the expectation.

^{**} p < 0.01.

Table 4

 $PM_{2.5} (\mu g/m^3)^{b}$:

Summary of multilevel logistic regression analyses (cross-classification of area and GP practice) in lowest and highest area SES quintiles; M1: separate analysis for each group of area variables, adjusted for age and gender; M2: all area variables, adjusted for age, gender and area level confounders. Only significant coefficients. N study population lowest SES quintile = 254,339; highest SES quintile = 252,108.

Area SES	Lowest SES quintile	Highest SES quintile
Social capital ^a : M1	High blood pressure (-) Depression (-) Asthma, COPD (-)	High blood pressure (-) Cardiac diseases (-) Coronary heart disease (-)
	Migraine, severe headache (-) MUPS (-) Diabetes (-)	Stroke, brain hemorrhage (-) Depression (-) Asthma, COPD (-) Migraine, severe headache (-) MUPS (-) Diabetes (-)
M2 Feelings of unsafety ^b :	Depression (-)	Diabetes (-)
M1	Coronary heart disease (+) Depression (+)	Cardiac diseases (+) Coronary heart disease (+)
	Migraine, severe headache (+) MUPS (+) Diabetes (+)	Stroke, brain hemorrhage (+) Anxiety disorder (+) Migraine, severe headache (+) MUPS (+) Diabetes (+)
M2	Coronary heart disease (+) Depression (+)	Cardiac diseases (+) Coronary heart disease (+) Stroke, brain hemorrhage (+) Anxiety disorder (+) MUPS (+) Diabetes (+)
Perceived crime frequency ^b : M1	High blood proceurs (+)	Depression (+)
MI	High blood pressure (+) Migraine, severe headache (+) MUPS (+) Pichetre (+)	Depression (+)
M2 Percentage green space ^a :	Diabetes (+) Depression (-)	
M1	High blood pressure (-)	Coronary heart disease (-)
	Cardiac diseases (-) Coronary heart disease (-) Stroke, brain hemorrhage (-) Depression (-) Anxiety disorder (-) Asthma, COPD (-) Migraine, severe headache (-) MUPS (-) Diabetes (-)	Depression (-) Anxiety disorder (-)
М2	High blood pressure (-) Stroke, brain hemorrhage (-) Depression (-) Anxiety disorder (-) Asthma, COPD (-) MUPS (-) Diabetes (-)	
$PM_{10}~(\mu g/m^3)^{~b}$: M1	High blood pressure (+) MUPS (+) Diabetes (+)	
M2 $PM_{-} = (\mu a/m^3)^b$		

Table 4 (continued)

Area SES	Lowest SES quintile	Highest SES quintile
M1		
M2	Depression (-)	
$NO_2 (\mu g/m^3)^b$:		
M1	High blood pressure (-) Asthma, COPD (-)	High blood pressure (-)
	Medically unexplained symptoms (-)	
M2	High blood pressure (-)	High blood pressure (-)
	Depression (-)	Diabetes (-)
	Anxiety disorder (-)	Migraine, severe
	-	headache (+)
	Asthma, COPD (-)	MUPS (-)
	MUPS (-)	
	Diabetes (-)	

^a Expected direction: negative coefficient (-).

Table 5

Summary of significant interaction effects in multilevel logistic regression analyses (cross-classification of area and GP practice), stratified by highest and lowest quintile of area SES; all area variables, adjusted for age, gender and area level confounders. N study population lowest SES quintile = 254,339; highest SES quintile = 252,108.

ICPC cluster	Area SES lowest quintile	Area SES highest quintile
High blood pressure	Social capital × greenspace ^{*a}	Unsafety feelings \times PM ₁₀ ^{*a}
	PM ₁₀ × greenspace *a	PM ₁₀ × greenspace **b
Cardiac disease	PM ₁₀ × greenspace ***a	PM ₁₀ × greenspace b
Coronary heart disease	PM ₁₀ × greenspace ***a	PM ₁₀ × greenspace b
Stroke, brain hemorrage	PM ₁₀ × greenspace ^{*a}	PM ₁₀ × greenspace**b
Depression	PM ₁₀ × greenspace**a	_
Anxiety disorder	_	_
Asthma, COPD	PM ₁₀ × greenspace *a	_
Migraine/severe headache	-	$PM_{10} \times greenspace^{**b}$
MUPS	_	PM ₁₀ × greenspace b
Diabetes	$PM_{10} \times greenspace^{**a}$	PM ₁₀ × greenspace**b

^{*} p < 0.05.

Looking from the angle of the morbidity clusters, there is not much pattern to discern. Stroke/ brain hemorrhage and depression both have two significant relationships in the adjusted models; the other morbidity clusters one or none at all.

3.3. Stratified analysis by area SES

As it turns out, the area level adjusters strongly attenuate the effects of the variables of interest. Separate stepwise analyses (not reported in tables) show that this is the result of adding area SES and the percentage of immigrants in an area. In areas with lower area SES and a higher percentage of immigrants, the prevalence of the morbidity clusters is higher. This might partly be the result of compositional effects that we could not control for by lack of individual variables on socioeconomic status and ethnicity. We therefore decided to stratify the analysis by area SES in quintiles. Comparing over the area SES quintiles, we see more significant effects in the lowest and in the highest quintile than in the intermediate quintiles. Table 4 therefore summarizes the results of the analyses for the highest and the lowest SES quintile and shows significant effects in the expected direction (i.e. lower morbidity for social capital and greenspace and higher morbidity for feelings of unsafety, perceived crime frequency and the air pollution

^b Expected direction: positive coefficient (+).

^{**} p < 0.01.

^a Sign of coefficient in expected direction.

b Sign of coefficient not in expected direction.

variables). The underlying coefficients for all quintiles are in Additional Tables A4–A13.

From this summary table we conclude the following.

More social capital coincides, as expected, with lower prevalence of morbidity in the baseline model (including age and sex) with social capital as the only area variable. However, most of the significant relations disappear with the inclusion of the other area variables. More feelings of unsafety and a higher perceived crime frequency in an area coincide, as expected, with higher prevalence of morbidity in the baseline model. For feelings of unsafety approximately half these relations remain significant in the adjusted model. However, for perceived crime frequency most relationships disappear.

For the indicators of the physical environment, the percentage of green space in areas coincides, against the expectations, with lower prevalence of morbidity in the baseline models. In the adjusted model especially the significant relations in the lowest quintile of area SES remain.

Looking at the same summary table from the morbidity angle, in the fully adjusted models (M2) the prevalence of cardiac disease has only one significant relationship in the expected direction with the area variables, in this case with feelings of unsafety in low SES areas. Prevalence of high blood pressure is lower in areas with more green-space, but also (against the expectations) in areas with more NO_2 pollution. Coronary heart disease is more prevalent in areas with more feelings of unsafety, as is stroke/ brain hemorrhage in the highest area SES quintile. Depression, MUPS and diabetes are most often significantly related to the area variables in the adjusted models.

The decrease in neighbourhood variance between the baseline model (including only age and sex) and the adjusted, stratified model (see Additional Table A3) was highest for the clusters depression and migraine/severe headache. For the cluster anxiety disorders the decrease was lowest.

3.4. Interactions between neighbourhood characteristics

In the previous steps we found more significant effects in the lowest and in the highest SES quintile. We therefore only tested for interactions in these SES quintiles. Moreover for area safety we decided only to look at unsafety feelings and for air pollution to PM_{10} . We distinguished alleviating effects, i.e. the interactions between green space and PM_{10} and between social capital and unsafety feelings and for these interactions we expected a negative coefficient; and reinforcing effects, i.e. the interactions between green space and social capital (expected direction: negative) and between PM_{10} and unsafety feelings (expected direction: positive) (Table 5).

From the summary table it appears that in the lowest area SES quintile all significant interactions are in the hypothesized direction. In the highest area SES quintile we found significant interactions in the opposite direction, with only one exception. However, the interpretation of these interactions is in many cases not straightforward. The reason is that many of the interactions with air pollution (PM $_{10}$) did not show a main effect in the expected direction. Only three of the significant interactions in the hypothesized direction had significant main effects of the separate variables, either in Model 1 or Model 2. This is the case for high blood pressure, where in the lowest area SES quintile social capital and greenspace seem to reinforce each other and where green space seems to alleviate the effect of air pollution; and for diabetes where the interaction also points to a alleviating effect of green space.

4. Discussion

4.1. Main results

This study showed that social capital, feelings of unsafety, perceived crime frequency and percentage of green space are related to the prevalence of nearly all morbidity clusters in models that only adjust for age and sex and that take in the area variables one by one. This confirms the findings of the existing literature. The variables indicating air pollution showed only few and mixed effects.

However, many of the separate effects disappear when neighbourhood level confounders are added. This was particularly the case for social capital and perceived crime frequency, but less so for green space and feelings of safety.

A stratified analysis by neighbourhood SES, partly as a proxy for individual socio-economic characteristics (that were not available in our data), roughly showed the same picture. We saw a tendency of more significant effects in the expected direction in the lowest and highest quintile of neighbourhood SES compared to the middle quintiles. In particular for the percentage of green space in neighbourhoods in the lowest SES quintile we saw associations with the prevalence of several groups of morbidity. This corroborates a previous analysis of greenspace and morbidity (Maas et al., 2009), while taking into account more area level confounders. Green space, as a health enhancing aspect of the physical environment, seems especially beneficial in low SES areas. Feelings of unsafety, as a health threatening aspect of the social environment, seem to be more robustly related to the prevalence of morbidity than social capital, as a health enhancing aspect of the social environment (comp. Ruijsbroek et al., 2016).

With our second research question we probed into interaction effects between the key environmental variables on the prevalence of morbidity. We found alleviating effects of green space on air pollution for the prevalence of high blood pressure and for diabetes. Given a negative relation of green space with the prevalence of these two conditions and a positive relation with air pollution (particulate matter PM_{10}), we found a negative effect of the interaction. We found a reinforcing effect of social capital and green space for the prevalence of high blood pressure. Given a negative relation of social capital and green space with the prevalence of this condition, we found a negative effect of the interaction.

4.2. Interpretation

The key variables in this analysis were taken from the four cells of the combination of physical and social influences and supposedly health enhancing and threatening influences (see Fig. 1). We started with separate models for each of these variables, only adjusted for age and sex, and then analyzed the combined (additive as well as interaction) effects of these neighbourhood variables, including a number of neighbourhood level confounders. The lack of clear relations of the air pollution variables with the prevalence of morbidity is probably related to the size of the neighbourhoods we used. Exposure to air pollution is highly dependent on e.g. closeness to main roads; the average based on areas of the size we used does not reflect the inter-area differences in exposure.

For the social aspects of the environment nearly all relationships with the prevalence of the morbidity clusters disappeared in the fully adjusted models. In our view, this does not mean that these characteristics of the social environment are not important for the prevalence of morbidity. The analysis might be over-adjusted. Especially the social aspects of the neighbourhood environment are part of a complex interplay with population characteristics, such as migrant status, and

individual and area level socio-economic status. To disentangle these relations in-depth studies and studies over time are important (Macintyre and Ellaway, 2003; Diez Roux, 2011; Sampson, 2012).

To reduce the number of possible interactions we only looked at two types of effects: reinforcing effects of two enhancing (greenspace and social capital) or threatening influences (feelings of unsafety and particulate matter PM_{10}) and alleviating effects of either social (social capital and feelings of unsafety) or physical influences (greenspace and particulate matter PM_{10}). In addition, we only tested interactions in the highest and lowest quintiles of area SES. Significant interaction effects in the hypothesized direction were nearly all found in low SES neighbourhoods, but in the absence of significant main effects of one of the constituting variables, these are difficult to interpret.

The health of people in low SES areas seems to be more affected by area characteristics, compared to people in high SES areas. Green space is related to the prevalence of morbidity, especially in low SES areas, whilst unsafety feelings are related to the prevalence of morbidity, especially in high SES areas. The alleviating effect of green space for negative effects of air pollution and the reinforcing effect of social capital and green space emphasize the importance of maintaining or increasing the (often small amount of) green space in low SES areas. Also, the effects of unsafety feelings in high SES areas deserve attention. Overall, we only found little clustering of morbidity in neighbourhoods in the baseline model. The largest neighbourhood variance is found for diabetes, comparable to the diabetes neighbourhood variance in a large Australian study (Astell-Burt et al., 2014), but much lower than in an urban neighbourhood study in Boston (Piccolo et al., 2015). In the analyses with all individual and area variables we found the largest reduction of variation between areas for the chance of having a depression and for having migraine/severe headache. In both cases the reduction of area level variance was 70%. Although this is a large reduction, it is large reduction of a relatively small higher level variance to begin with. The smallest reduction we found for the chance of having an anxiety disorder, where we could explain only one fifth of the variation between areas.

4.3. Limitations and strengths of the study

A limitation of our study is that we had few (only age and sex) individual level characteristics that might be related to the prevalence of morbidity. The confounding effects of area SES and percentage immigrants might at least partly be individual, compositional effects. Another limitation is that we used a limited number of operationalisations of the key environmental variables. Measurement error of these variables might have led to attenuation of the exposure-response relationships.

We used 4-digit postal code of the areas where people live as neighbourhoods. People also spend time and have activities at other places, such as schools or work, and are exposed to environmental influences during their daily trajectories (Vallée et al., 2010; Chaix et al., 2013). However, if we include the time people spend sleeping – during which they are still exposed to environmental influences (Zanobetti et al., 2010; Astell-Burt et al., 2013; Hale et al., 2013; Bassett and Moore, 2014) – the largest part of the day is spent at home (European Communities, 2004). Although the living environment is not the only context in which people are exposed, it is a relevant context. The size of the neighbourhoods is, however, a weakness of this

study. Especially for the variables related to air pollution the areas are too big to estimate exposure at home. More generally, there is no consensus on how to operationalize neighbourhood and depending on the phenomenon of interest a different spatial scale may be relevant.

Finally, since our study was cross-sectional we cannot draw conclusions about causality.

Among the strong aspects of our study is that we used nationwide data on the Netherlands, including nearly half of Dutch neighbourhoods in terms of 4-digit postal code areas. The selection might be slightly biased against neighbourhoods with smaller population size as a result of the policy of Statistics Netherlands to only provide data on neighbourhoods with more than three or four respondents for the surveys we used to calculate aggregated neighbourhood characteristics. The selection was further determined by the coverage of the NIVEL Primary Care Database as the source of information on morbidity. There is a slight over-representation of participating practices in strongly urbanized areas and under-representation in rural areas. However, the description of the study population in terms of individuals and neighbourhoods showed no big differences with the situation of the Netherlands as a whole.

Furthermore, we used morbidity as assessed by GPs as our outcome measures. Other studies have used self-rated health or self-reported illness. In the Dutch health care system, virtually the whole population is registered with a particular GP/practice. For most health problems GPs are the first health professional to consult and there is very little spatial variation in terms of distance to the nearest practice. A practice is almost always available within 15 min driving time. Consequently, GP-data give a good picture of morbidity in the population, reflecting health problems that warranted a visit to a GP. Especially in the case of MUPS, there are people with these symptoms that did not visit their GP. However, using GP assessed morbidity results in clear health endpoints, although perhaps slightly underestimating the relationship. We took the structure of the data into account by cross-classifying the neighbourhood where people live and the GP practice they are listed at.

In addition, the area level independent variables were measured as close as possible to 2013 – the year of the morbidity data. We adjusted the analyses for neighbourhood confounders that may be related to the prevalence of morbidity. The number of neighbourhoods was such that there was no problem with degrees of freedom at the neighbourhood level.

Last but not least, we analyzed specific interactions between the key variables at neighbourhood level. Usually only cross-level interactions are studied; however, in this study we analyzed interactions between neighbourhood characteristics. That is to our best knowledge not often done.

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Appendix A

See Fig. A1.

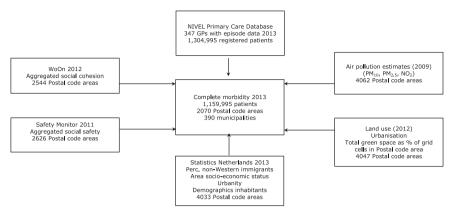


Fig. A1. Flow chart of the combination of data sources and resulting number of patients, postal code areas and municipalities.

See Tables A1-A13.

 ${\bf Table~A1}$ Correlations (Spearman's r) between all neighbourhood characteristics (N = 2070).

ICPC cluster	Social Capital	Feelings of unsafety	Perceived crime frequency	Percentage green space	PM_{10} in $\mu g/m^3$	$PM_{2.5}$ in $\mu g/m^3$	NO_2 (µg/ m^3)	Population density	Area SES	Percentage immigrants
Social capital	1.00	-0.46 [*]	-0.48*	0.46	-0.37 [*]	-0.22*	-0.39	-0.46 [*]	0.25*	-0.54*
Feelings of unsafety		1.00	0.76	-0.48	0.47	0.36	0.48	0.50*	-0.38*	0.68
Perceived crime frequency			1.00	-0.58	0.64	0.43*	0.67*	0.64*	-0.22*	0.76
Percentage green space				1.00	-0.58*	-0.30 [*]	-0.65*	-0.71*	0.15*	-0.61*
PM ₁₀ in μg/m ³					1.00	0.72^{*}	0.83	0.62*	-0.04	0.64
$PM_{2.5}$ in $\mu g/m^3$						1.00	0.56	0.34*	-0.03	0.38
$NO_2 (\mu g/m^3)$							1.00	0.67*	0.06*	0.65
Population density								1.00	-0.15^{*}	0.68
Area SES									1.00	-0.39*
Percentage										1.00
immigrants										

^{*} p < 0.01.

Table A2 Correlation of the prevalence of the disease clusters aggregated to neighbourhood level (N = 2070).

ICPC cluster	High blood pressure	Cardiac disease	Coronary heart disease	Stroke, brain hemorrage	Depression Anxiety disorde	Anxiety disorder	Asthma, COPD	Asthma, COPD Migraine/severe headache	Medically Unexplained Physical Symptoms	Diabetes
High blood pressure Cardiac disease Coronary heart disease Stroke, brain hemorrage Depression Anxiety disorder Asthma, COPD Migraine/severe headache Medically Unexplained Physical Symptoms Diabetes	1.00	1.00	0.27 0.57 1.00	0.16 0.22 0.21 1.00	-0.03 -0.01 -0.01 -0.03 1.00	-0.03 -0.01 -0.02 -0.00 -0.01 1.00	0.05 0.13 0.11 0.05 -0.02 1.00	0.05 0.05 0.07 0.09 0.09 0.04 1.00	0.13 0.11 0.08 0.16 0.10 0.05 -0.01 0.27 1.00	0.31 0.19 0.09 0.19 0.19 -0.00 0.04 0.03 0.14

* p < 0.01 ** p < 0.05

Variances in baseline and full cross-classified multilevel models and percentage change in variance (N_{municipalities} = 390; N_{neighbourhoods} = 2070; N_{GP practices} = 347; N_{Study population} = 1,159,929); logistic regression – dependent variable: having a disease episode in an ICPC cluster.

ICPC cluster	Baseline model: variance at			Full model: variance at			% reduction in neighbour-	
	Municipality	Neighbourhood	GP Practice	Municipality	Neighbourhood	GP Practice	hood variance	
High blood pressure	0.008	0.012	0.057	0.01	0.009	0.057	25%	
Cardiac disease	0.004	0.013	0.037	0.004	0.010	0.037	23%	
Coronary heart disease	0.007	0.018	0.063	0.005	0.012	0.062	33%	
Stroke, brain hemorrage	0.02	0.013	0.039	0.02	0.008	0.037	38%	
Depression	0.019	0.017	0.068	0.007	0.005	0.070	71%	
Anxiety disorder	0.008	0.016	0.093	0.002	0.013	0.091	19%	
Asthma, COPD	0.009	0.007	0.071	0.006	0.004	0.071	43%	
Migraine/severe headache	0.010	0.010	0.028	0.008	0.003	0.024	70%	
Medically Unexplained Physical Symptoms	0.005	0.009	0.054	0.006	0.004	0.051	56%	
Diabetes	0.012	0.045	0.041	0.004	0.017	0.029	62%	

Table A4 Multilevel logistic regression analysis (cross-classification of area and GP practice); M1: separate analysis for each group of area variables, adjusted for age and gender; M2: all area variables, adjusted for age, gender and area level confounders (B-coefficients). N study population lowest quintile = 254,339; 2nd quintile = 247,104; 3rd quintile = 222,137; 4th quintile = 184,241; highest quintile = 252,108.

ICPC cluster	High blood pressure				
Area SES	Lowest quintile	2nd quintile	3nd quintile	4nd quintile	Highest quintile
Social capital:					
M1	-0.330*	0.058	-0.065	-0.120	-0.444*
M2	-0.037	0.142	-0.024	-0.085	-0.218
Feelings of unsafety:					
M1	0.004	0.032	-0.043	0.014	0.104*
M2	-0.024	0.001	-0.033	-0.008	0.068
Perceived crime frequency:					
M1	0.053	0.001	0.046	0.033	0.015
M2	0.017	-0.019	0.029	-0.001	0.040
Percentage green space:					
M1	-0.002*	-0.0003	-0.0002	-0.0005	0.0002
M2	-0.002	-0.001	-0.0003	-0.0005	-0.0001
PM_{10} in $\mu g/m^3$:					
M1	0.047**	-0.018	0.011	0.016	0.017
M2	0.033	-0.015	0.006	0.014	0.021
$PM_{2.5}$ in $\mu g/m^3$:					
M1	-0.017	0.016	-0.040	-0.060**	0.005
M2	-0.016	0.016	-0.039	-0.058**	-0.003
$NO_2 (\mu g/m^3)$:					
M1	-0.010*	0.001	-0.001	0.002	-0.009**
M2	-0.011*	0.002	-0.002	0.002	-0.011*

p < 0.01

 ^a Baseline models are only adjusted for age and sex of the patients
 ^b Full models contain the (groups of) area characteristics of interest, stratified by area SES, and are adjusted for age and sex of the patients and area covariates (Model M2 in Additional Tables A4-A13).

p < 0.05

Multilevel logistic regression analysis (cross-classification of area and GP practice); M1: separate analysis for each group of area variables, adjusted for age and gender; M2: all area variables, adjusted for age, gender and area level confounders (B-coefficients). N study population lowest quintile = 254,339; 2nd quintile = 247,104; 3rd quintile = 222,137; 4th quintile = 184,241; highest quintile = 252,108.

ICPC cluster	Cardiac diseases				
Area SES	Lowest quintile	2nd quintile	3nd quintile	4nd quintile	Highest quintile
Social capital:					
M1	0.018	0.07	-0.306	-0.197	-0.396 [*]
M2	0.171	0.108	-0.263	-0020	-0.118
Feelings of unsafety:					
M1	0.056	-0.026	0.002	0.047	0.192**
M2	0.059	-0.045	-0.015	0.033	0.185**
Perceived crime frequency:					
M1	-0.001	0.032	0.042	0.023	0.004
M2	-0.004	0.043	0.005	-0.027	-0.012
Percentage green space:					
M1	-0.0014*	-0.0006	-0.0009	-0.0011	-0.0012
M2	-0.0014	-0.0009	-0.0003	-0.00009	-0.0003
PM_{10} in $\mu g/m^3$:					
M1	0.023	-0.038	-0.010	0.019	-0.004
M2	0.015	-0.038	-0.005	0.030	0.0002
$PM_{2.5}$ in $\mu g/m^3$:					
M1	-0.044	0.022	0.014	0.001	0.002
M2	-0.042	0.033	0.011	-0.005	-0.025
$NO_2 (\mu g/m^3)$:					
M1	-0.002	0.005	0.003	-0.001	0.003
M2	-0.006	-0.0002	-0.001	-0.004	-0.001

^{*} p < 0.05

Table A6 Multilevel logistic regression analysis (cross-classification of area and GP practice); M1: separate analysis for each group of area variables, adjusted for age and gender; M2: all area variables, adjusted for age, gender and area level confounders (B-coefficients). N study population lowest quintile = 254,339; 2nd quintile = 247,104; 3rd quintile = 222,137; 4th quintile = 184,241; highest quintile = 252,108.

ICPC cluster	Coronary heart diseases						
Area SES	Lowest quintile	2nd quintile	3nd quintile	4nd quintile	Highest quintile		
Social capital:							
M1	-0.279	0.081	-0.133	-0.137	-0.590°		
M2	0.154	0.282	-0.336	0.178	-0.206		
Feelings of unsafety:							
M1	0.121*	-0.006	-0.005	0.058	0.201*		
M2	0.109^{*}	-0.061	-0.019	0.039	0.159*		
Perceived crime frequency:							
M1	0.030	0.050	0.026	0.045	0.016		
M2	0.015	0.032	-0.013	-0.024	0.003		
Percentage green space:							
M1	-0.0027^{*}	-0.001	0.0002	-0.0016**	-0.0017**		
M2	-0.0009	-0.0006	0.0024**	-0.0004	-0.0006		
PM_{10} in $\mu g/m^3$:							
M1	0.027	-0.079*	-0.021	-0.042	-0.039		
M2	0.007	-0.083*	0.007	-0.037	-0.034		
$PM_{2.5}$ in $\mu g/m^3$:							
M1	-0.034	0.058	0.030	0.055	0.063		
M2	-0.032	0.072^{*}	-0.002	0.050	0.035		
$NO_2 (\mu g/m^3)$:							
M1	0.0001	0.014**	0.004	0.011	0.004		
M2	-0.008	0.009	0.0007	0.006	-0.002		

^{*} p < 0.01

p < 0.01

p < 0.05

Multilevel logistic regression analysis (cross-classification of area and GP practice); M1: separate analysis for each group of area variables, adjusted for age and gender; M2: all area variables, adjusted for age, gender and area level confounders (B-coefficients). N study population lowest quintile = 254,339; 2nd quintile = 247,104; 3rd quintile = 222,137; 4th quintile = 184,241; highest quintile = 252,108.

ICPC cluster	Stroke, brain hemorrage						
Area SES	Lowest quintile	2nd quintile	3nd quintile	4nd quintile	Highest quintile		
Social capital:							
M1	-0.129	-0.170	-0.119	-0.604*	-0.687*		
M2	0.147	-0.026	-0.032	-0.300	-0.422		
Feelings of unsafety:							
M1	0.027	0.051	0.032	0.087	0.294*		
M2	0.035	-0.005	0.014	0.045	0.267^{*}		
Perceived crime frequency:							
M1	0.040	0.029	0.038	0.76	-0.000		
M2	0.043	-0.014	0.048	0.030	0.007		
Percentage green space:							
M1	-0.0026**	-0.0016	-0.0006	-0.0031*	-0.0007		
M2	-0.002*	-0.0007	0.0001	-0.0027**	0.0003		
PM_{10} in $\mu g/m^3$:							
M1	0.005	-0.046	-0.051	-0.026	-0.005		
M2	0.001	-0.035	-0.040	-0.044	0.006		
$PM_{2.5}$ in $\mu g/m^3$:							
M1	-0.007	0.085**	0.090**	0.063	0.067		
M2	-0.010	0.081**	0.079*	0.076	0.026		
$NO_2 (\mu g/m^3)$:							
M1	0.003	0.009	0.005	0.008	-0.001		
M2	-0.003	0.007	0.001	-0.001	-0.007		

^{*} p < 0.05

Table A8 Multilevel logistic regression analysis (cross-classification of area and GP practice); M1: separate analysis for each group of area variables, adjusted for age and gender; M2: all area variables, adjusted for age, gender and area level confounders (B-coefficients). N study population lowest quintile = 254,339; 2nd quintile = 247,104; 3rd quintile = 222,137; 4th quintile = 184,241; highest quintile = 252,108.

ICPC cluster Area SES	Depression						
	Lowest quintile	2nd quintile	3nd quintile	4nd quintile	Highest quintile		
Social capital:							
M1	-0.743*	-0.306	-0.126	-0.389	-0.585^{*}		
M2	-0.443*	-0.004	0.201	0.110	-0.267		
Feelings of unsafety:							
M1	0.125	0.100**	0.004	0.126*	0.072		
M2	0.079**	0.071	-0.008	0.095**	0.031		
Perceived crime frequency:							
M1	0.019	0.059**	0.074**	0.066	0.094*		
M2	-0.082^{*}	0.027	0.016	-0.011	0.046		
Percentage green space:							
M1	-0.005*	-0.003*	-0.002*	-0.003*	-0.003^{*}		
M2	-0.004*	-0.000	-0.0006	-0.001	-0.0016		
PM_{10} in $\mu g/m^3$:							
M1	0.041	-0.025	-0.013	0.028	-0.008		
M2	0.019	-0.022	-0.016	0.007	0.0005		
$PM_{2.5}$ in $\mu g/m^3$:							
M1	-0.044	0.012	0.020	-0.017	0.064		
M2	-0.056**	-0.002	0.025	0.007	0.053		
NO_2 ($\mu g/m^3$):							
M1	-0.002	0.011**	0.006	0.003	0.003		
M2	-0.008**	0.003	0.0004	-0.003	-0.006		

^{*} p < 0.01

p < 0.01

p < 0.05

Multilevel logistic regression analysis (cross-classification of area and GP practice); M1: separate analysis for each group of area variables, adjusted for age and gender; M2: all area variables, adjusted for age, gender and area level confounders (B-coefficients). N study population lowest quintile = 254,339; 2nd quintile = 247,104; 3rd quintile = 222,137; 4th quintile = 184,241; highest quintile = 252,108.

ICPC cluster Area SES	Anxiety disorder						
	Lowest quintile	2nd quintile	3nd quintile	4nd quintile	Highest quintile		
Social capital:							
M1	-0.111	-0.358^{1}	-0.570^{2}	-0.337	-0.280		
M2	-0.023	-0.161	-0.218	-0.037	-0.143		
Feelings of unsafety:							
M1	0.033	0.019	0.050	0.003	0.109^{1}		
M2	0.015	-0.015	0.027	-0.017	0.106^{1}		
Perceived crime frequency:							
M1	-0.016	0.056^{1}	0.055	0.069	-0.031		
M2	-0.044	0.007	-0.006	-0.003	-0.056		
Percentage green space:							
M1	-0.002^{2}	-0.003^{2}	-0.003^{2}	-0.003^{2}	-0.002^{1}		
M2	-0.002^{1}	-0.001	-0.001	-0.001	-0.001		
PM_{10} in $\mu g/m^3$:							
M1	0.018	-0.004	0.039	-0.024	0.011		
M2	0.008	-0.012	0.025	-0.035	0.022		
$PM_{2.5}$ in $\mu g/m^3$:							
M1	0.012	-0.001	-0.025	0.017	-0.039		
M2	0.012	0.005	-0.002	0.020	-0.049		
$NO_2 (\mu g/m^3)$:							
M1	-0.006	0.008	0.001	0.012^{1}	0.002		
M2	-0.009^{1}	0.0001	-0.007	0.006	-0.004		

 $[\]begin{array}{c} ^{1} \ p < 0.05 \\ ^{2} \ p < 0.01 \end{array}$

Table A10 Multilevel logistic regression analysis (cross-classification of area and GP practice); M1: separate analysis for each group of area variables, adjusted for age and gender; M2: all area variables, adjusted for age, gender and area level confounders (B-coefficients). N study population lowest quintile = 254,339; 2nd quintile = 247,104; 3rd quintile = 222,137; 4th quintile = 184,241; highest quintile = 252,108.

ICPC cluster	Asthma, COPD						
Area SES	Lowest quintile	2nd quintile	3nd quintile	4nd quintile	Highest quintile		
Social capital:							
M1	-0.227*	0.135	-0.246	-0.161	-0.263*		
M2	-0.024	0.184	0.087	0.070	-0.098		
Feelings of unsafety:							
M1	0.028	0.023	-0.010	0.018	0.056		
M2	0.006	0.019	-0.018	-0.001	0.038		
Perceived crime frequency:							
M1	0.032	0.015	0.092**	0.068**	0.022		
M2	0.010	0.021	0.041	0.003	0.002		
Percentage green space:							
M1	-0.002**	-0.001	-0.002**	-0.002**	-0.001		
M2	-0.0014*	-0.0004	-0.0001	-0.0006	0.0001		
PM_{10} in $\mu g/m^3$:							
M1	0.019	-0.036*	0.006	-0.022	-0.006		
M2	0.003	-0.033*	-0.001	-0.027	0.0004		
$PM_{2.5}$ in $\mu g/m^3$:							
M1	-0.002	0.010	-0.024	0.001	-0.008		
M2	0.004	0.009	-0.013	0.011	-0.011		
$NO_2 (\mu g/m^3)$:							
M1	-0.007*	0.005	0.006*	0.010**	0.002		
M2	-0.010**	0.001	0.003	0.007*	0.0003		

Table A11

Multilevel logistic regression analysis (cross-classification of area and GP practice); M1: separate analysis for each group of area variables, adjusted for age and gender; M2: all area variables, adjusted for age, gender and area level confounders (B-coefficients). N study population lowest quintile = 254,339; 2nd quintile = 247,104; 3rd quintle = 222,137; 4th quintile = 184,241; highest quintile = 252,108.

ICPC cluster	Migraine, severe headache						
Area SES	Lowest quintile	2nd quintile	3nd quintile	4nd quintile	Highest quintile		
Social capital:							
M1	-0.561**	0.075	-0.115	-0.132	-0.514**		
M2	0.029	0.372*	0.158	0.224	-0.147		
Feelings of unsafety:							
M1	0.069*	0.010	-0.051	0.117**	0.090*		
M2	0.018	-0.011	-0.053	0.081**	0.073		
Perceived crime frequency:							
M1	0.091**	0.051*	0.097**	0.030	0.029		
M2	0.020	0.015	0.060	-0.041	0.006		
Percentage green space:							
M1	-0.003**	-0.001*	-0.001	-0.002**	-0.001		
M2	-0.0006	-0.0005	0.0004	-0.0015	-0.0003		
PM_{10} in $\mu g/m^3$:							
M1	0.024	-0.006	-0.018	-0.036	-0.038		
M2	0.001	-0.012	-0.026	-0.053**	-0.036		
$PM_{2.5}$ in $\mu g/m^3$:							
M1	-0.022	0.010	0.007	0.013	-0.036		
M2	-0.014	0.021	0.018	0.035	-0.034		
$NO_2 (\mu g/m^3)$:							
M1	0.005	0.004	0.007	0.012**	0.009*		
M2	-0.001	0.001	0.004	0.010*	0.009*		

Table A12
Multilevel logistic regression analysis (cross-classification of area and GP practice); M1: separate analysis for each group of area variables, adjusted for age and gender; M2: all area variables, adjusted for age, gender and area level confounders (B-coefficients). N study population lowest quintile = 254,339; 2nd quintile = 247,104; 3rd quintile = 222,137; 4th quintile = 184,241; highest quintile = 252,108.

ICPC cluster	Medically unexplained symptoms						
Area SES	Lowest quintile	2nd quintile	3nd quintile	4nd quintile	Highest quintile		
Social capital:							
M1	-0.333**	-0.024	0.0154	-0.160	-0.390**		
M2	0.078	0.066	0.088	0.075	-0.145		
Feelings of unsafety:							
M1	0.042*	0.009	-0.032	0.040	0.114**		
M2	0.006	-0.031	-0.035	0.021	0.084**		
Perceived crime frequency:							
M1	0.054**	0.019	0.084**	0.048*	0.002		
M2	0.007	-0.007	0.056**	-0.001	-0.002		
Percentage green space:							
M1	-0.003**	-0.001**	-0.001*	-0.002**	-0.0005		
M2	-0.002**	-0.002**	0.0002	-0.001	0.000		
PM_{10} in $\mu g/m^3$:							
M1	0.034*	-0.020	0.004	-0.018	0.010		
M2	0.017	-0.023	0.002	-0.027	0.019		
$PM_{2.5}$ in $\mu g/m^3$:							
M1	-0.011	0.015	0.007	0.013	-0.028		
M2	-0.005	0.023	0.016	0.028	-0.028		
$NO_2 (\mu g/m^3)$:							
M1	-0.007**	0.0005	-0.0002	0.004	-0.003		
M2	-0.011**	-0.003	-0.004	0.001	-0.006		

Table A13 Multilevel logistic regression analysis (cross-classification of area and GP practice); M1: separate analysis for each group of area variables, adjusted for age and gender; M2: all area variables, adjusted for age, gender and area level confounders (B-coefficients). N study population lowest quintile = 254,339; 2nd quintile = 247,104; 3rd quintile = 222,137; 4th quintile = 184,241: highest quintile = 252,108.

ICPC cluster Area SES	Diabetes						
	Lowest quintile	2nd quintile	3nd quintile	4nd quintile	Highest quintile		
Social capital:							
M1	-1.280**	-0.195	-0.503*	-0.726**	-1.360**		
M2	-0.151	0.245	-0.068	-0.022	-0.812**		
Feelings of unsafety:							
M1	0.167**	0.047	0.051	0.105	0.242**		
M2	0.036	-0.027	-0.002	0.009	0.128**		
Perceived crime frequency	ı:						
M1	0.119**	0.058*	0.066	0.092*	0.033		
M2	-0.029	-0.012	-0.062	-0.051	-0.006		
Percentage green space:							
M1	-0.007**	-0.002**	-0.002**	-0.004**	-0.001		
M2	-0.002**	-0.0005	0.0004	-0.002**	0.0009		
PM_{10} in $\mu g/m^3$:							
M1	0.075**	0.007	0.034	0.021	0.014		
M2	0.023	-0.010	0.018	-0.034	0.015		
$PM_{2.5}$ in $\mu g/m^3$:							
M1	-0.049	-0.009	-0.013	-0.041	0.037		
M2	-0.032	0.009	-0.010	-0.0002	0.036		
$NO_2 (\mu g/m^3)$:							
M1	-0.002	0.004	0.002	0.009	-0.008		
M2	-0.015**	-0.004	-0.004	0.002	-0.014**		

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