Environmental Research 166 (2018) 290–297

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

# More green space is related to less antidepressant prescription rates in the Netherlands: A Bayesian geoadditive quantile regression approach

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ARTICLE INFO

*Keywords:*
Mental health
Antidepressants
Exposures
Green space
Quantile regression
Spatial epidemiology

ABSTRACT

*Background:* Exposure to green space seems to be beneficial for self-reported mental health. In this study we used an objective health indicator, namely antidepressant prescription rates. Current studies rely exclusively upon mean regression models assuming linear associations. It is, however, plausible that the presence of green space is non-linearly related with different quantiles of the outcome antidepressant prescription rates. These restrictions may contribute to inconsistent findings.
*Objective:* Our aim was: a) to assess antidepressant prescription rates in relation to green space, and b) to analyze how the relationship varies non-linearly across different quantiles of antidepressant prescription rates.
*Methods:* We used cross-sectional data for the year 2014 at a municipality level in the Netherlands. Ecological Bayesian geoadditive quantile regressions were fitted for the 15%, 50%, and 85% quantiles to estimate green space–prescription rate correlations, controlling for physical activity levels, socio-demographics, urbanicity, etc.
*Results:* The results suggested that green space was overall inversely and non-linearly associated with antidepressant prescription rates. More important, the associations differed across the quantiles, although the variation was modest. Significant non-linearities were apparent: The associations were slightly positive in the lower quantile and strongly negative in the upper one.
*Conclusion:* Our findings imply that an increased availability of green space within a municipality may contribute to a reduction in the number of antidepressant prescriptions dispensed. Green space is thus a central health and community asset, whilst a minimum level of 28% needs to be established for health gains. The highest effectiveness occurred at a municipality surface percentage higher than 79%. This inverse dose-dependent relation has important implications for setting future community-level health and planning policies.

## 1. Introduction

Interest among both researchers and health policymakers in the mental health pathway of environmental exposure has grown substantially (Tost et al., 2015; Helbich, 2018; Gascon et al., 2015; van den Bosch and Sang, 2017; Gong et al., 2016). One reason for this is that neuropsychiatric conditions, such as depression, are now among the leading disease burdens globally (World Health Organization, 2013; Steel et al., 2014). This is of particular concern in the Netherlands, where the lifetime prevalence of depression is high (19%) (De Graaf et al., 2010).

Demographic factors, lifestyles, and household characteristics explain some, but not all, variation in depression prevalence (Mair et al., 2008; Richardson et al., 2015; Blair et al., 2014; Kinderman et al., 2015). There is much debate about the contribution of natural environments, such as green space (e.g., parks and woodland), within people's residential environment (Gascon et al., 2015). Findings that the presence of green space is among the determinants of people's mental health converge (van den Bosch and Sang, 2017; Nieuwenhuijsen et al., 2017; Markevych et al., 2017). Although not consistently confirmed across experimental and epidemiological research, several cross-sectional (van den Berg et al., 2015; de Vries et al., 2016; Nutsford et al., 2013; Triguero-Mas et al., 2017; Groenewegen et al., 2018; McEachan et al., 2016; Cox et al., 2017) and a few longitudinal studies (Tomita et al., 2017; Astell-Burt et al., 2014; Alcock et al., 2014; Gariepy et al., 2014) show that green space exposures protect against the development and onset of poor mental health (Hartig et al., 2014).

Because the mechanisms between green space and depression appear to be complex, the underlying pathways are under debate. Proposed interrelated mechanisms include, but are not limited to, green space restoring attention, supporting stress recovery and physical

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https://doi.org/10.1016/j.envres.2018.06.010
Received 22 April 2018; Received in revised form 16 May 2018; Accepted 6 June 2018
0013-9351/ 

activity, and stimulating social interaction (Nieuwenhuijsen et al., 2017; Markevych et al., 2017; Hartig et al., 2014; Kaplan, 1995). Empirical studies (van den Berg et al., 2015; Nutsford et al., 2013; Picavet et al., 2016) testing these mechanisms typically rely on multiple-choice self-reported rating scales, instead of diagnostic interviews, to examine depression symptoms. This might provoke self-reporting response bias (Rosenman et al., 2011) and challenge comparability across studies through the availability of numerous depression screeners. This is accompanied by a lack of coherence in cut-off points to distinguish between mild, moderate, and severe depression (Manea et al., 2012).

These issues might be addressed by the use of objective health indicators such as medication prescription rates (Rowlingson et al., 2013). Antidepressant medication is widely utilized for depression treatment (Fournier et al., 2010; Blüml et al., 2017) and represents an ideal proxy for depression prevalence (Schofield et al., 2016). Apart from two contradictory studies in the UK (Taylor et al., 2015; Gidlow et al., 2016), little is known about how green space is related to antidepressant prescription rates. However, such associative studies are more complicated than they seem at first sight. Linear mean regressions are fitted as standard methodology (van den Berg et al., 2015; Triguero-Mas et al., 2017; Tomita et al., 2017; Picavet et al., 2016; Gidlow et al., 2016). Lacking theoretical foundation (Markevych et al., 2017; Hartig et al., 2014), there is no plausible reason for such a simplification linking green space only to the conditional mean of the response variable (e.g., antidepressant prescription rates), which may over- or underestimate or incorrectly assume that no correlation exists (Cade and Noon, 2003). To our knowledge, there is no research on how green space affects mental health for points other than the mean of the response distribution. Yet, it is rational to assume that the upper, central, and lower quantiles of the response variable may be affected differently by green space and may depend on different risk and protective factors. Bayesian geoadditive quantile regression (BQR) (Kneib, 2013; Waldmann et al., 2013), which had not previously been applied in green space research, could provide valuable insights into other distributional features of the response that could not be uncovered with mean regressions. BQR also has the ability to account for non-linear effects on the quantiles and, importantly, is able to account for unobserved spatial correlations. Non-linear dose-response functions (Shanahan et al., 2016) make intuitive sense because, for example, people living in areas with a high prevalence of depression (indicated by high prescription rates) may have different risk factors and exposures, and may benefit more from green space than those residing in healthier areas with lower prescription rates. That the functional form of green space is more complicated than linear was shown (Klompmaker et al., 2018). As area-level prescription data are spatially patterned (Rowlingson et al., 2013; Helbich et al., 2015), unexplained spatial correlations needs to be incorporated into BQR, otherwise regression estimates will be biased (Lawson, 2013).

The paucity of antidepressant rate–green space studies coupled with methodological concerns indicated a research need. We made a contribution to existing research by investigating the associations between the amount of green space and antidepressant prescription rates per municipality in the Netherlands. In order to pay particular attention to how the associations might vary across different quantiles, we applied BQR for the first time. We generated the following hypotheses: 1) The more green space in a municipality, the lower the antidepressant prescription rate, and 2) the strength of the association differs across the quantiles in a non-linear fashion. A more thorough understanding of this association may contribute to lower pharmaceutical spending on treating mental and behavioral disorders.

## 2. Materials and methods

### 2.1. Study background

As the Netherlands is among the top spenders on mental healthcare in the Organization for Economic Cooperation and Development (OECD) (Statistics Netherlands, 2015; OECD, 2017), we undertook the study in this country by means of a cross-sectional, ecological research design. The study was conducted at the municipality level to comply with privacy regulations and because this was the most detailed level where all data were accessible. We selected all 403 municipalities for 2014. Municipalities varied not only in size (median = 6,495 ha; min. = 696; max. = 50,569), but also in population size (median = 25,691 people; min. = 942; max = 810,937).

### 2.2. Data

#### 2.2.1. Antidepressant prescription rates

Depression prevalence, our outcome variable, was operationalized by means of antidepressant prescription rates per 1,000 inhabitants per municipality in the year 2014 (de Graaf-Ruizendaal and de Bakker, 2013). Our data represent antidepressant medication prescribed by general practitioners (GPs), who are the first point of contact to treat symptoms of depression in the Dutch healthcare system. The antidepressants (N06A) are classified according to the Anatomical Therapeutic Chemical Classification System codes that GPs record per patient contact and include, for example, Selective Serotonin Reuptake Inhibitors such as Prozac. The antidepressant records were extracted from the Demand Supply Analysis Monitor (Vraag Aanbod Analyze Monitor) from the Primary Care Database 2014 (Zwaanswijk et al., 2009), maintained by the Netherlands Institute for Health Services Research. The database comprised 391 GP practices with 1541,902 listed patients. Municipalities with missing data on antidepressant prescriptions (N = 19) were excluded.

#### 2.2.2. Green space

The primary exposure variable of interest was green space. Given our ecological research design and the numerous ways to define green space (Klompmaker et al., 2018), we defined green space as the proportion of green space per municipality (in %). Data on green space were gathered from the most recent Dutch land use database for the year 2012/13 (Hazeu, 2014). We extracted and aggregated land use classes referring to parks, agricultural areas, forests, etc. using a geographic information system (de Vries et al., 2016; Helbich et al., 2018).

#### 2.2.3. Confounders

For each municipality we collected nine confounders, informed by previous research. The data were uniformly aggregated to the municipality level. Unless stated otherwise, data comprised routinely collected information for 2014 obtained from Statistics Netherlands.

*2.2.3.1. Demographics*. Other studies have reported differences in mental disorders between the native population and migrants (Missinne and Bracke, 2012). We therefore controlled for the proportion of non-Western people per municipality (in %). Because depression risk also varies across age cohorts, and older adults are at greater risk (Blazer and Hybels, 2005), we adjusted for the proportion of elderly people (in %).

*2.2.3.2. Socioeconomic status*. The absence of labor market participation may diminish a person's social status and increase the risk for depression (Musić Milanović et al., 2015). We considered the unemployment rate (in %) among those aged 15–75 years. Neighborhood deprivation has also been shown to be correlated with depression (Mair et al., 2008). In order to adjust for area-based deprivation, we included the average housing value (in 1,000 euros). We assumed that deprived areas are at higher risk and have noticeably higher antidepressant prescription rates.

*2.2.3.3. Health status and healthcare*. Physical activity protects against depressive disorders (Mammen and Faulkner, 2013). We used data on