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Spatial patterns in the rate of alcohol withdrawal syndrome in Galicia (Spain)

Jenifer Espasandín-Domínguez[a]*, Ipek Guler[a], María P. Pata[a],

Francisco Gude[b], Arturo González-Quintela[c], Carmen Cadarso-Suárez[a]

[a] *Unit of Biostatisctics, School of Medicine, University of Santiago de Compostela. Santiago de Compostela, 15782, Spain*
[b] *Hospital Clínico Universitario. Clinical Epidemiology Unit. Santiago de Compostela, 15782, Spain.*
[e] *Hospital Clínico Universitario. Department of Internal Medicine. Santiago de Compostela, 15782, Spain.*

Abstract

In the last twenty years there have been many studies that have considered geographic area as a health determinant. The analysis of the impact of these geographical effects is of importance to capture possible spatial heterogeneities. The present ecological study was aimed at investigating spatial trends in the rate of alcohol withdrawal syndrome (AWS rate) in a defined community. To take into account other potential confounding factors, we used Structured Additive Regression (STAR) models with Poisson response, which allows flexible modeling of spatial and non-linear effects. The analysis showed different results of various socio-demographic effects on the response when including the spatial trends in the model.

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Keywords: Structured Additive Regression; Penalized splines; sociodemographic effects; AWS; Poisson.

* Jenifer Espasandín-Domínguez. Tel.: 881812283; fax: +34-981-54.71.72.
E-mail address: jenifer.espasandin@rai.usc.es

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1. Introduction

In a survey from 2012, 66% of Spanish adults older than fifteen years reported alcohol consumption in the previous year, and 5% of this population are at greater risk of suffering other serious diseases (Encuesta Nacional de Salud. España 2011/12 [1]). In addition, heavy drinkers may develop alcohol dependence, which alters drinking behavior to alleviate withdrawal symptoms and a need for increased amounts of alcohol to achieve intoxication American Psychiatric Association [2].

Alcohol Withdrawal Syndrome (AWS) is a frequent cause for hospital admission in Spain. Due to the lack of data about the epidemiology of AWS, in 2011 Gonzalez-Quintela et al. [3] published a paper to investigate spatio-temporal trends in the rate of AWS in Galicia and potentially associated socio-demographic factors. For this purpose, rates of AWS per district and ecological predictors of AWS cases were analyzed separately by means of Generalized Additive Models (GAM, Hastie and Tibshirani [4]) with Poisson response.

In this study, to investigate spatial trends in the rate of AWS, we re-analyze these data but using Structured Additive Regression (STAR, Fahrmeir et al. [5]) models with Poisson response, which allows flexible modeling of spatial and non-linear effects.

2. Methods

2.1 Data base

This ecological study was performed in Galicia, an autonomous region located in the northwest of Spain. We included all discharges from public hospitals (January 1996 to December 2006) with the diagnosis of AWS (ICD-9-CM code numbers 291.8, 291.0 and 291.3). The total number of the patients included in the study was 7195.

We included socio-demographic variables, aggregated per district and restricted to the population aged 16 years and older, obtained from the Spanish National Institute of Statistics: *education level* (*edu)* calculated as the mean score of studies of individuals in each district, *socio-economic level (socio)*, calculated as the mean socio-economic score of the household reference person (Table 1); *unemployment rate* (*unemploy*), calculated as the percentage of working-age people who are seeking employment; and *rate of activity (activity)*, calculated as the percentage of people aged 16 years or older who are economically active. We also included spatial effects in order to demonstrate the clinical impressions about the influence of the geographical trends in the rate of AWS.

2.1. Statistical methodology

STAR models with Poisson response, including spatial structures are used to study the AWS rate. The STAR methodology represents an extension of the classical GAM regression models, commonly used in this environmental context. Their advantage lies on the flexibility of including spatial and temporal covariates, jointly with the other continuous covariates information. In our study, the STAR model is as follows:

$$\eta = offset(\log(population)) + f_1(unemploy) + f_2(socio) + f_3(activity) + f_4(edu) + f_{spat}(s) + b(s),$$

where η is the number of AWS's cases; $f_1,...,f_4$ are unknown, smooth functions for modeling continuous covariates, $f_{spat}(s)$ represents correlated spatial effects of region s, and b_s denotes uncorrelated unstructured spatial effects. By estimating both structured and unstructured components, we can distinguish between possible strong

Table 1. Scoring of the level of studies and socio-economic level according to the Spanish National Institute of Statistics (www.ine.es).

Level of studies		*Socio-economic levels*	
Status	*Score*	*Status*	*Score*
No education	0	Unemployed people seeking their first job or inactive people	0
Elementary education (< 5years)	1	Unemployed people	0.5
Unfinished primary education (5-9 years)	2	Retired or institutionalized people	1
Completed primary education (~10 years)	2.5	Workers in agriculture, service, industry, and other no skilled workers	1
Secondary education (~12 years)	3	Small businessmen in agriculture (with no employees) and members of agrarian cooperatives	1.5
First degree vocational training or university education	3.5	Businessmen in agriculture (with employees); members of no agrarian cooperatives; clerks, overseers, and skilled no agrarian workers; military	2
University education (≥4 years)	4	Directors of farms, small businessmen in no agrarian business (with no employees), civil servants, technicians working as employees	2.5
Doctoral Thesis	4.5	Businessmen in no agrarian business (with employees), self-employed technicians and professionals, general managers, government administrators	3

spatial structures and others patterns present only locally. Finally, the model was adjusted for the size of each district population by incorporating the logarithm of the population size as an offset term.

Inference for STAR models can be carried out using either full Bayes methods or empirical Bayes (EB) techniques, the latter used in this study. In EB inference, variance -or smoothing parameters- are considered unknown constants. They are estimated using restricted maximum likelihood (REML). To model continuous covariates, cubic P-splines (Eilers and Marx [6]) are used with 20 equidistant knots and a second order random walk prior.

For the correlated spatial effects, we assume the simplest spatial smoothness prior for the function evaluations, $\gamma_s = f_{spat}(s) : \gamma_s | \gamma_r, r \neq s \sim N\left(\frac{1}{N_s} \sum_{r \in \delta_s} \gamma_r, \frac{\tau^2_{spat}}{N_s} \right)$, where $N_s = |\delta_s|$ is the number of adjacent sites or neighbors and $r \in \delta_s$ denotes that region r is a neighbor of site s. Here, the (conditional) mean of γ_s is an un-weighted average of function evaluations of neighboring sites. The prior is a generalization of a first random walk called Markov Random field (MRF, Fahrmeir et al. [7]).

Suppose $s \in \{1,\ldots,S\}$ is a cluster variable indicating to which particular group observation b_s belongs, a common approach to solve the problems of unobserved heterogeneity is to assume a standard Gaussian random effect prior, that is, $b_s \sim N(0, \tau^2), s = 1,\ldots,S$.

The prior specification is completed by assuming that all parameters are conditionally independent. The analysis was conducted using BayesX (Brezger et al. [7]) statistical software, freely available online from www.bayesx.org.

2.2. Results

Results of the fitted models are presented in Table 2. Based on several information criteria (AIC, BIC, GCV), better results are obtained after including spatial effects.

Table 2: Akaike information criterion (AIC), Bayesian information criterion (BIC), and generalized cross-validation (GCV) taking into spatial effect or not.

Models	2xlog-likelihood	Degrees of freedom	AIC	BIC	GCV
Without spatial effects	-40029.6	45.8481	-39937.9	-39766.1	7.36371
With spatial effects	-41458.1	163.492	-41131.1	-40518.7	3.50782

The estimated smooth effects for both models are shown in Figure 1 and 2. We can see that the effects of the continuous covariates become smoother after including the spatial effects into the model. As can be seen in these figures, the effects of the continuous covariates are similar in both models. Spatial effects are shown in Figure 3. The most noteworthy aspect of including spatial effects is that the rate of AWS per district was unevenly distributed. We observed that low rates are present in large cities. The clusters with the highest rates corresponded most often to rural districts.

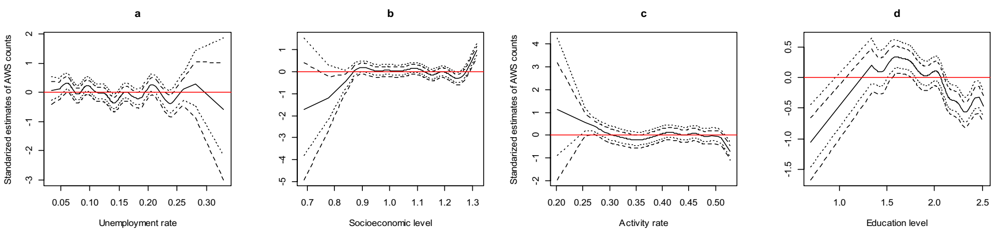

Figure 1. AWS data: Shown are the posterior modes (together with 95% and 80% pointwise credible intervals) between the rate of alcohol withdrawal syndrome (AWS) and socio-demographic variables: socio-economic level (a), employment rate (b), occupational activity rate (c), and education level (d) without taking into account spatial effects.

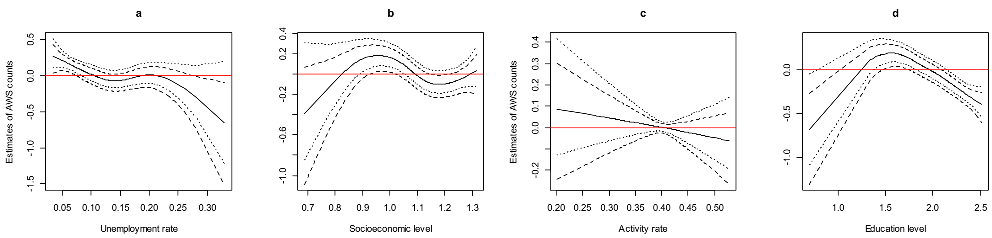

Figure 2. AWS data: Shown are the posterior modes (together with 95% and 80% pointwise credible intervals) between the rate of alcohol withdrawal syndrome (AWS) and socio-demographic variables: socioeconomic level (a), employment rate (b), occupational activity rate (c), and education level (d).

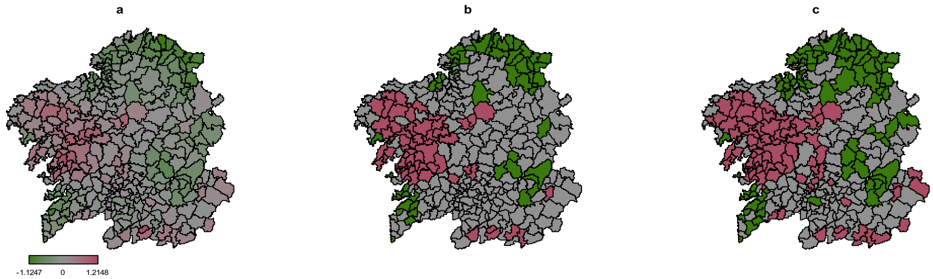

Figure 3. AWS data: Spatial structured effects of municipality. Shown are the posterior modes (a), and the posterior probabilities for a nominal level of 95% (b) and 80% (c). Unstructured effects were non-significant.

Discussion

The present study indicates that the rate of severe AWS is independently associated with education level in this defined population. This association shows a non linear shape with highest AWS rates in those municipalities with an average educational score of about one (< 5 years), with decreasing rates as the educational level goes up. This association underlies the uneven geographical distribution and clustering of AWS rates in this defined community. Taken together, these results may help to establish priorities in preventive measures.

When the spatial variability is analyzed here there is evidence that the effect of the educational level on AWS rates continue to exist even after other potential risk factors have been taken into account. In addition, the relationship between educational level and AWS rate is smoother when geographic area is entered as a health determinant.

Acknowledgments

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