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REGIONAL FACTORS HINDERING TUBERCULOSIS SPREAD IN ROMANIA. EVIDENCE FROM A SEMIPARAMETRIC GWR MODEL

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Abstract

While hastily celebrating the downwards trend in the emergence of new tuberculosis (TB) cases, most researchers overlooked not only several unsolved medical problems, but also the high local inequalities and diverging territorial trends of this disease in Romania. Our paper fills this gap in the literature by analysing how specific local factors impact on TB incidence, with a focus on healthcare infrastructure, captured through a custom made composite index. Aiming to address properly the spatial dimension of the phenomenon, we used a semiparametric (mixed) geographically weighed regression (GWR) model, which is especially valuable in this context as it brings additional information regarding the variation of factors across the country. The results confirm the importance of healthcare endowment in countering the spread of TB and enable a better understanding of the specific influence of local characteristics.

Keywords: geographically weighed regression, tuberculosis, healthcare, Romania.

JEL Classification: I14, R15, R23.

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1. Introduction

The vast majority of health-related research is understandably performed at individual level, in order to identify the direct factors of influence. Nevertheless, macro-level factors can be relevant as well, as they target larger socio-economic influences not entirely visible at micro-level. This perspective is especially important for contagious diseases, such as tuberculosis (e.g. Wei et al., 2016). Tuberculosis (TB) is a severe infectious bacterial disease and its significant incidence and prevalence in Romania recommends it for a thorough investigation, including its territorial enablers and inhibitors. This approach provides useful insights that might help alleviate TB's harmful effects and rein in future spread, since such information is more useful for central and local decision makers, compared to micro data that is relevant mostly to medical practitioners.

Our paper belongs to the macro data strand of healthcare research and, by focusing on the spatial dimension of tuberculosis incidence, fills an important gap in the Romanian literature on TB. Starting from the correlation between tuberculosis and socio-economic status, as proven in literature (e.g. Olson et al., 2012), we examine various factors that might impact on the territorial distribution of TB. For this endeavor we employ up to date spatial techniques, able to capture properly the spatial dimension of TB incidence. The geographically weighed regression (GWR) model is especially valuable in this context as it brings additional information regarding the variation of factors across the country, thus enabling a better understanding of the specific influence of local characteristics.

The rest of this paper is structured as follows. In the next section we analyze the regional incidence and prevalence of tuberculosis in Romania and potential factors of influence, as identified by previous studies. Section 3 introduces the GWR model, explaining its special features and the advantages related to a more in depth analysis of spatial variation of factors. Details on the construction of a special healthcare composite index and the rest of the explanatory variables are also provided in this section. Section 4 is dedicated to the discussion of the results from the GWR model and their implications in terms of health regional policy. Section 5 concludes by summarizing the main findings and discussing limitations of present research, as well as opportunities for future ones.

The novelty of this study lays in introducing specific spatial analysis techniques that can enhance the understanding of socio–economic factors that impact on the incidence of tuberculosis in Romania, thus providing a solid ground to further inform public interventions.

2. Regional incidence and prevalence of tuberculosis and potential factors of influence

Tuberculosis is a severe and potentially fatal infectious bacterial disease that affects mainly the lungs. Its prevalence continues to remain significant in Romania, although the emergence of new cases is constantly declining, a trend which was maybe too hastily labeled "a success story" (Marica, 2009).

Why is tuberculosis still a problem? On one hand, although the incidence of tuberculosis in Romania steadily diminished over the last fifteen years, its treatment success rate and detection rate remained roughly stable, while the death rate displayed but a very weak decline (Figure 1). On the other hand, an alarmingly high number of patients became multidrug-resistant (de Colombani et al., 2014). In a European context, Romania records the most cases that no longer respond to treatment (Maguire, 2016).

Accounting for about 25% of the total number of tuberculosis patients in the European Union (The Economist, 2015), having the highest incidence rate (de Colombani et al., 2014), as well as one of the lowest healing rates (Romanian Govern, 2014), Romania holds an uncomfortable TB top place in Europe. Therefore, the scale and the particularities of TB incidence and prevalence in Romania are still a matter of concern at European level, triggering many analyses and reports (The Economist, 2015; Maguire, 2016; "Tuberculosis surveillance and monitoring in Europe 2016 Report", etc.).

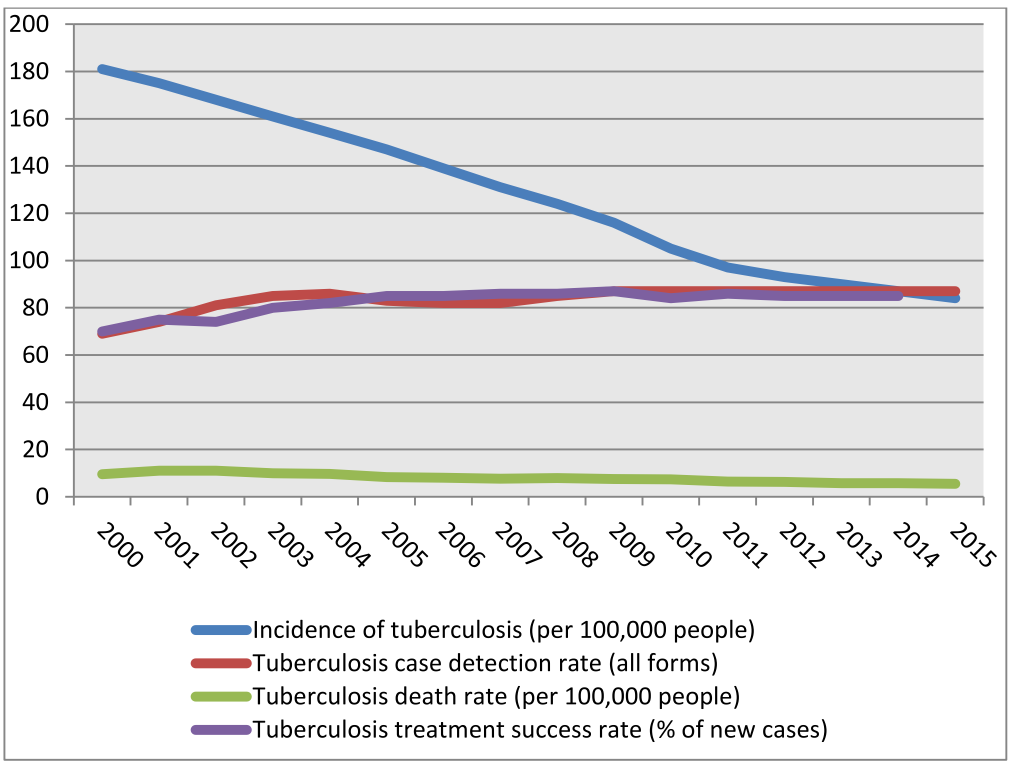

Figure 1. Tuberculosis statistics for Romania, 2000-2015
Source: own processing based on World Bank data (2017)

National strategies and programs, with ambitious goals, have been devised to deal with this issue, from the National Tuberculosis Programme 1997-2000 to the National Strategy for Curbing Tuberculosis in Romania for the period 2015-2020 (Romanian Govern, 2014). While some of them proved to be really effective (Marica, 2009), the results are not entirely satisfactory and many problems, mainly related to insufficient funding and poor healthcare infrastructure, still remain to be solved (World Health Organisation, 2011; de Colombani et al., 2014; The Economist, 2015).

An aspect generally overlooked so far is the territorial distribution of tuberculosis in Romania. The overall decline trend in TB incidence at aggregate country level can mask high local inequalities and diverging territorial trends. The regional distribution of tuberculosis shows high regional variation in Romania (Figure 2), its incidence ranging in the year 2014 from a minimum of 2.39 cases per 10000 inhabitants in Bucharest municipality to a maximum of 37.51 cases in Tulcea County.

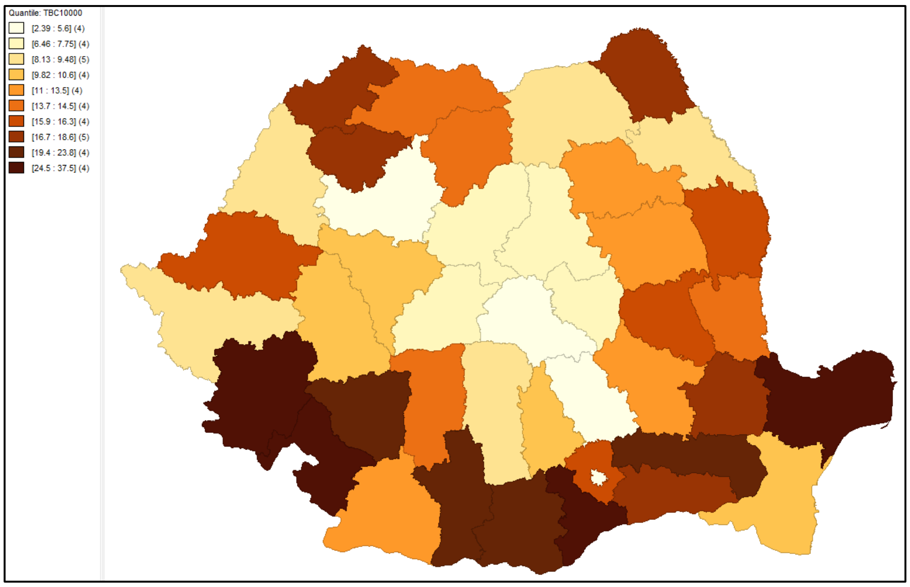

Figure 2. Spatial distribution of tuberculosis incidence per 10000 inhabitants

Source: own processing based on National Institute of Statistics data (2017)

The correlation between tuberculosis and socio-economic status is a largely discussed topic in the literature (Olson et al., 2012; Santos et al. 2007; Gupta et al. 2004) and researchers strongly agree on its importance. This correlation has been proved to vary geographically, and numerous factors have been found responsible for it.

While medical conditions like diabetes mellitus, chronic liver diseases, malignancy, chronic kidney diseases or malnourishment proved to be associated with pulmonary tuberculosis, (Gupta et al. 2011), risk factors like gender and age are also of a high importance (Kolappan, 2007), and the TB incidence tends to be associated not only with patients' demographic characteristics, but also with workplaces, certain environmental factors, poverty and socioeconomic status. Pan et al. (2015) and Aggarwal (2009) prove that medical workers are prone to TB infections more than other categories. Factors such as pollution, alcohol abuse, insufficient education, low income levels, and history of homelessness (Narasimhan et al. 2013, Kawatsu and Ishikawa, 2014) also play an important role in the spread of this disease. A significant stream of research has been conducted in developing countries, as for example Berhe et al. (2013) in Ethiopia, Cremers et al.

(2016) in Zambia or Sandhu (2011) in India, but the concern holds even in developed countries like for example Japan (Kawatsu and Ishikawa, 2014). In all cases the relation between socioeconomic factors and the disease cannot be ignored, although some of the studies led to unclear results.

Another important direction in exploring the impact of various factors on tuberculosis incidence is the access to affordable health services (Zhang, 2007), but also the infrastructure aiming to foster the prevention through primary healthcare (Bulgarelli et al., 2017). The structure of in – country health care delivery systems has also been discussed as being related to the effective delivery of TB treatment (Institute of Medicine, US 2009), while Floyd et al. (2016) stress the idea that infrastructure should come into play only after the clinical and public health criteria are used. Most of these studies address low or middle – income countries, providing ground for taking into consideration infrastructure – related variables in our study as well.

The last dimension in this preliminary discussion of the literature points to the fact that previous studies on the relation between TB and socioeconomic factors vary not only in the variables chosen to explain TB incidence, or number of deaths from TB, but also in methods. Although all these studies share the same characteristic in that they used data at patient level, and in many cases they were based on multilevel, or mixed models, in some cases the variables are employed as they are, while in other cases composite indices are preferred. The use of composite indices related to healthcare infrastructure led sometimes to unclear results (see for example Scoeman et al., 1991), but in the meantime using the raw variables as such can be a challenge either for multicollinearity reasons, or for the effects a higher number of variables has on the degrees of freedom in a regression model.

Setting all this information as a point of departure, the next section will introduce the model and the variables we decided to use, and will present a particular instrument – geographically weighted regression – as our main methodological tool in explaining the Romanian data related to TB incidence and its potential predictors.

3. Model and variables

The geographically weighted regression (GWR) model has constantly gained popularity in spatial analyses over the last two decades (Brunsdon et al., 1996; Fotheringham and Brunsdon, 1999; Fotheringham et al., 2002; Wheeler and Tiefelsdorf, 2005) and it has recently begun to be employed in healthcare research as well (e.g. Nakayaet al., 2005; Wei et al., 2016).

The main advantage of GWR, making it especially attractive in regional studies, is the ability to estimate regression coefficients that vary from one territorial unit to another. The real spatial patterns can be captured by these local coefficients and the phenomena can be better explained, compared to OLS global models.

The standard GWR model is represented as follows:

$$y_i(l) = \beta_{0i}(l) + \beta_{1i}(l)x_{1i} + \beta_{2i}(l)x_{2i} + ... + \beta_{ni}(l)x_{ni} + \varepsilon_i, \quad (1)$$

where y is the dependent and x_1 to x_n stand for the explanatory variables. The main particularity of this model is that the intercept and all beta coefficients are specific to each location l. The position of location l is determined based on its geographic X and Y coordinates.

Estimation of the beta coefficients of the GWR model (Charlton and Fotheringham, p. 1):

$$\hat{\beta}(l) = (X^T W(l) X)^{-1} X^T W(l) y \quad (2)$$

needs a special weights matrix *W(l)* for every location *l*. The estimation of model's parameters is based on a weighting procedure that allocates lower weights as distance from the point of reference increases. This allows capturing the declining influence in space of more distant territorial units.

Usual options for kernel weights computation are bi-square or Gaussian, in both "fixed" and "adaptive" form. The adaptive Gaussian weights steadily decrease while moving away from the central point, without ever becoming null:

$$w_{ij} = \exp\left(-\frac{d_{ij}^2}{\Delta_{i(k)}^2}\right) \quad (3)$$

where the values d_{ij} stand for Euclidean distances of the observations j from location i. Of special importance for the estimations is $\Delta_{i(k)}^2$ representing the adaptive bandwidth. It measures the distance to the k nearest neighbor. The usual selection criterion for choosing this bandwidth is Akaike.

The adaptive bi-square procedure clearly discriminates between declining weights up to a certain threshold $\Delta_{i(k)}^2$:

$$w_{ij} = \left(1 - \frac{d_{ij}^2}{\Delta_{i(k)}^2}\right)^2 \text{ for } d_{ij} < \Delta_{i(k)}^2 \quad (4)$$

and null values corresponding to a distance over that threshold: $w_{ij} = 0$ if $d_{ij} > \Delta_{i(k)}^2$.

Not only the GWR model provides larger statistic performance compared to global OLS model, it also enables a deeper understanding of the factors of influence, based on their local estimations. A variant of the standard GWR is the semiparametric (mixed) model that reunites global and local coefficients in the same specification, as follows:

$$y_i(l) = \beta_{0i}(l) + \beta_{1i}(l) x_{1i} + \beta_{2i}(l) x_{2i} + ... + \beta_{ni}(l) x_{ni} + \alpha_1 z_{1i} + +\alpha_2 z_{2i} + ... + \alpha_m z_{mi} + \varepsilon_i, \quad (5)$$

where the α coefficients of the new explanatory variables z are geographically invariable, in contrast to the varying β coefficients of the initial explanatory variables x.

The advantage of the latter specification is that it accommodates variables having both low and high geographical variation, while reducing the estimation complexity and therefore enhancing the overall performance. A special testing procedure is applied to discriminate between global and local coefficients, depending on the geographical variability of each regressor.

As usual, variable selection for the model was guided by the findings in previous empirical research, within the limits of available statistical data. Aiming to improve the estimations by encompassing as much information as possible, but without using too many variables (that would drastically reduce the degrees of freedom), we developed a new synthetic indicator of healthcare infrastructure capturing both material and human conditions. Our composite index draws on official Romanian healthcare statistics available at county level and captures critical factors for population health.

While calculating this synthetic measure of health infrastructure in Romania, we followed the standard method to build composite indices (OECD, 2008). We selected the main variables that reflect material and human resources engaged in healthcare (see Table 1 for the description of variables). The complexity of the healthcare sector requires a diversity of variables, quantitative and qualitative, to reflect accurately the spatial inequalities in the relevant factors of influence, but our endeavour is limited by the information currently available in official statistics.

Table 1. The variables for the GWR model

VARIABLES	MEASUREMENT
Composite Index of Healthcare Infrastructure	*Normalised values*
1.Synthetic Index of Physical Medical Infrastructure	*Normalised values*
Number of hospitals Hospital beds Medical offices in schools	*Number*
2.Synthetic Index of Human Medical Infrastructure	*Normalised values*
Number of physicians in public sector Number of physicians in private sector Medical nurses	*Number*
Socio-economic and demographic explanatory variables	
GDP per capita	*Thou RON/ inhabitant*
Average net monthly earnings	*RON/employee*
Life expectancy at birth	*years*
Urbanisation rate	*%*
Unemployment rate	*%*
Population growth	*%*
Population density	*Inhabitants per square km*

The initial variables have undergone a standardisation procedure, and have been further assigned to groups according their different nature: material factors (hospitals, hospital beds, medical offices in schools) and human factors (physicians in public sector and in private sector, medical nurses). Two synthetic indices that highlight these two dimensions of healthcare infrastructure have been computed as simple arithmetic means of the previously standardised values.

Finally, the composite index of healthcare infrastructure is obtained as mean of the two synthetic indices, giving higher weigh to the human factor, essential for the correct diagnosis and treatment of tuberculosis.

The value of the composite index could rank between a minimum of 0, if a certain county records the lowest performance for all variables, and a maximum of 1, if the same county is on top position for all variables.

Additional explanatory variables will be included in the model to capture various social, economic and demographic conditions that might influence the regional incidence of tuberculosis (Table 1). The selected variables are spatially relevant, displaying considerable variation among Romanian counties.

The data for our analysis came from the National Institute of Statistics and the Public Health Institute. All variables are recorded at county (NUTS3) level, for the year 2014.

4. Results and discussion

In order to be able to discriminate correctly between local and global coefficients, we started the analysis with a test of geographical variability for all our potential explanatory variables.

Based on positive values of AICc difference criterion, the results displayed in Table 2 show that three variables (life expectancy, logarithm of GDP per capita and population growth) display insufficient territorial variation for the GWR local estimation. It implies that these variables should be kept in the model as global coefficients. All other variables are appropriate for local (county level) coefficient estimations.

We used a Gaussian model with an adaptive bi-square kernel and Cartesian coordinates given by the Euclidean distance. The method employed for finding best bandwidth dimension was interval search and the criterion used in this process was AICc. We also applied the option for standardisation of independent variables.

Table 2. Results from the geographical variability test

Variable	F	DOF for F test		DIFF of Criterion
Unemployment rate	0.235469	1.440	0.662	-36103.01002
Health composite index	0.537297	1.470	0.662	-28602.40263
Urbanisation rate	0.327357	1.872	0.662	-9046.332850
Life expectancy	0.655227	1.292	0.662	73296.55984
Log of GDP/cap	0.553440	1.083	0.662	10945.71297
Average wage	184.0290	2.209	0.662	-6799.192287
Population growth	0.386489	0.998	0.662	7556.806132
Population density	1.260643	2.108	0.797	-6728.586397

The comparative results from OLS and GWR regressions forcefully illustrate the advantages of the latter. Estimations of the coefficients for composite healthcare index vary from a minimum of minus 3.114022 to a maximum of minus 1.250788, according to local conditions, instead of a fixed minus 1.901361 provided by Global OLS. Moreover, estimations also improved from a statistic point of view (table 3, columns 3 and 4).

Table 3. Parameter estimations from OLS and GWR regressions

Variable	**Minimum**	**Lower Quartile**	**GWR Mean (std. error)**	**OLS global coefficient (std. error)**	**Upper Quartile**	**Maximum**
0	*1*	*2*	*3*	*4*	*5*	*6*
Geographically varying (local) coefficients						
Intercept	11.740875	12.393404	13.680571*** (1.535025)	14.543054*** (0.894531)	15.093033	16.956980
Composite healthcare index	-3.114022	-2.177198	-1.872868*** (0.498725)	-1.901361* (1.02409)	-1.492173	-1.250788
Geographically fixed (global) coefficient						
Life expectancy			-3.98874*** (1.068918)	-4.137063*** (1.090194)		
Statistics (GWR against OLS)						
AICc			271.1060	272.7465		
Adjusted R-squared			0.619393	0.49382		
Model improvement						
			SS	F		
Global Residuals			1309.684			
GWR Improvement			324.893			
GWR Residuals			984.792	2.0962		

The geographical variation in coefficient levels (Figure 3) brings useful information regarding the specific impact of healthcare endowment in each county, thus guiding the appropriate design of local healthcare policies.

As expected, the negative sign of the coefficients for the composite index variable confirm the effects of better healthcare infrastructure for limiting the spread of TB in Romania.

The local estimates of the composite healthcare index, displayed in the map in Figure 3, illustrate their variation across the counties. A striking feature of this spatial distribution is the North-South and East-West decline in the absolute values of the coefficients estimated for the composite healthcare index. Keeping in mind that the composite index exerts a negative impact on tuberculosis and comparing its pattern of spatial variation with the distribution of TB new cases in Figure 2, we found that the healthcare infrastructure tends to influence stronger the regions with higher TB incidence. This raises hopes that the beneficial effects of improving healthcare endowment in less developed counties might have a powerful impact on curbing tuberculosis incidence in the future.

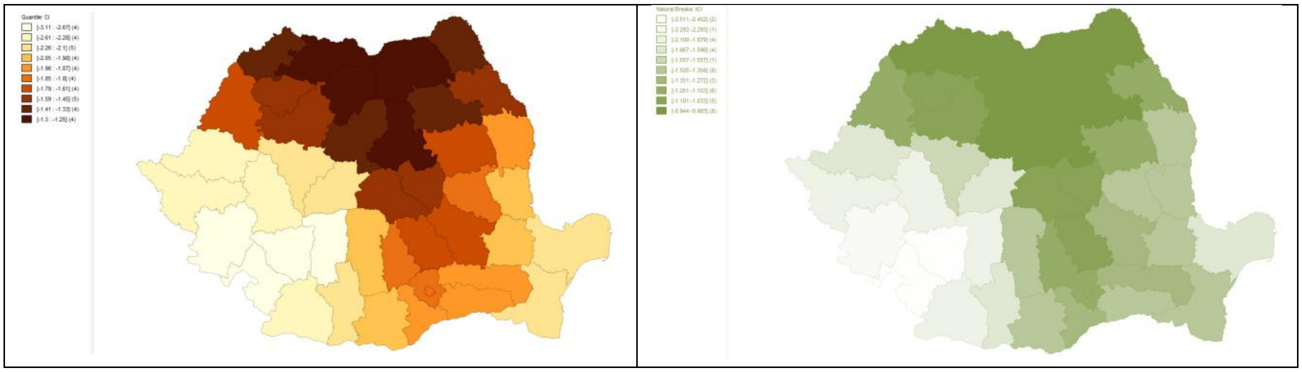

Figure 3. Estimations of composite index coefficients by county and associated significance (t stat)
Source: own processing

Given the pressure put by GWR requirements regarding the volume of data needed for efficient model estimation, we had to severely limit the number of regressors in the final specification. Although we tested all variables presented in Table 1, separately and in various combinations, and although several other regressors demonstrated statistical significance, our final choice was directed towards life expectancy, based on both highest significance level and highest explanatory relevance. Life expectancy is an important factor of influence, as it encompasses a wide array of medical, social, economic and demographic influences. It largely reflects the well-being of the population, shaped by specific economic conditions (development level, incomes, housing endowments and utilities, working conditions, etc.), demographic factors (gender and age structure), and, equally important, the health status. In this semiparametric GWR model, life expectancy has the expected negative sign and is highly significant. Since it displays lower territorial variance, it was estimated as a fixed (geographically invariant) coefficient and the GWR model provided only a global estimate for it.

The map in Figure 4 illustrates the variation of local R squared across counties. It shows that the explanatory power of the model, although fairly high in all counties, is significantly greater in Eastern, Western and especially in Southern counties, compared to the Center. The spatial increase in local R squared from center to periphery and from North to South mirrors a similar increase in TB incidence per 10000 inhabitants (see Figure 2).

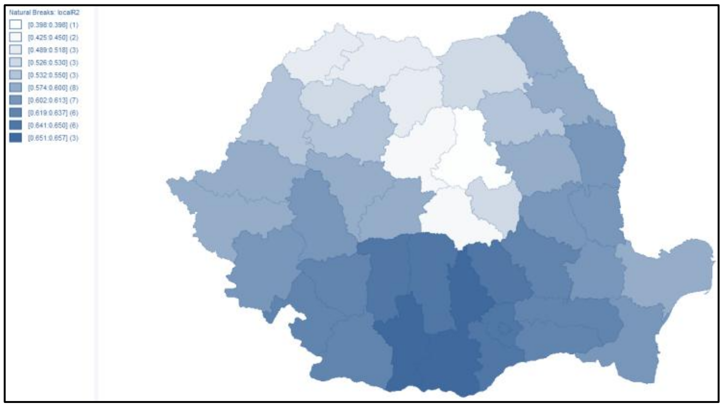

Figure 4. Local R squared
Source: own processing

The added value of estimating the GWR model instead of a global OLS model is clearly visible in the statistics displayed in Table 3. Lower GWR residuals against the OLS ones, smaller AICc and bigger R squared, all plead in favor of the geographically varying coefficients.

5. Summary and final remarks

In this paper we illustrated some of the computational advantages of introducing the GWR model in the healthcare research, with a direct focus on tuberculosis, a disease that has a well-known spatial component. The relatively low number of territorial units in our analysis conflicts with the large data requirement of GWR. Given the wide array of potential factors of influence, while selecting the explanatory variables for our model, the challenge was to find and retain only the most relevant regressors. Our solution was to reunite various indicators related to human capital and material conditions in the healthcare sector into a composite index that allows us to account for all of them without losing too many degrees of freedom.

Statistical data regarding the regional variation of TB incidence in Romania reveal clearly marked spatial differences. We tested various potential factors of influence on the territorial spread of TB, aiming to identify the most powerful socio-economic factors that inform its spatial distribution in Romania. Employing a semiparametric GWR model, we found that both our specially designed composite index of healthcare and the life expectancy are highly relevant and exert a negative impact on TB incidence, but only the former has geographically significant variance.

Our study is only a first step in the direction of introducing spatial techniques in the tuberculosis research area. It was meant to highlight the large computational opportunities brought about by spatial data science and, hopefully, to stimulate further TB research at territorial level.

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