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Opioid Mortality in the US: Quantifying the Impact of Key Determinants Using a Spatial Panel Data Approach

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Abstract: This paper employs a spatial Durbin panel data model, an extension of the cross-sectional spatial Durbin model to a panel data framework, to estimate the impact of a set of demographic and economic factors on state-level opioid-related mortalities in the US. The empirical model uses a pool of US states over six years from 2014 to 2019 and a nearest-neighbor matrix that represents the topological structure between the states. Calculation of direct (own state) and indirect (cross-state spillovers) effects estimates – based on Bayesian estimation and inference – reflects a proper interpretation of the marginal effects for our nonlinear model that involves lags of the dependent variable vector. The study provides evidence for the existence of spatial effects working through the dependent variable vector and points to the importance of larger indirect effects of *Asian* and *Hispanic/Latino* minorities on the one side and the population age groups *35-44 years* and *65 years and older* on the other. This finding echoes the first law of geography that *"everything is related to everything else, but near things are more related than distant things"* (Tobler 1970). Space – largely neglected in previous research – matters for gaining a valid and better understanding of why and how neighboring states contribute to opioid-related mortality in the states.

JEL: C23, I19, O51

Keywords: Spatial Durbin panel data model, Bayesian econometrics, Markov Chain Monte Carlo, direct (own state) effects, indirect (cross-state spatial spillover) effects, inferential statistics

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1 Introduction

Opioid-induced deaths (hereafter, briefly opioid mortality) increased sharply in the United States (US) during the past two decades, and opioid overdose mortality has become a pressing health problem today (Kopel 2019).[1] Commonly, the opioid epidemic is perceived as a rural, white problem (Sobotka and Stewart 2020). This perception stems from opioid epidemics in rural Appalachia (Schalkoff et al. 2020) and the substantial increase in overdose mortality rates in rural counties (see, for example, Rossen et al. 2013). But opioid rates tend to be similar or even higher in urban areas (Monnat 2019) and have started to increase in recent years for Blacks (Alexander et al. 2018). Nationally, from 2016 to 2017, the opioid death rate for Blacks increased by 25 percent compared to 11 percent for Whites (Keturah and Ayana 2018).

In response to the increasing opioid problem, a substantial scholarly literature has appeared. This literature reflects a diverse variety of perspectives, methodologies and data. Our paper shifts interest on demographic and economic factors that influenced opioid mortality across regions. Previous research investigating the determinants have examined the relationship between mortality and explanatory variables in a cross-sectional setting, but largely ignored the spatial dependence problem. [2] Spatial dependency is an unneglectable issue in aggregate level analysis, omitting which increases the risk of obtaining biased estimation results (see Baltagi et al. 2007). Only very few studies used spatial econometric techniques to control for spatial dependence among observational units such as regions. The most prominent examples include Sparks and Sparks (2010) and Yang et al. (2015) who apply spatial autoregressive and spatial Durbin models of US county mortality rates, respectively. These cross-sectional studies, however, lack a longitudinal perspective, and fail to account for temporal and spatial dependence simultaneously.

To overcome this shortcoming, we use panel data rather than cross-sectional data to study the relationship between mortality and explanatory variables. The use of panel data results in more accurate inference of model parameters. Panel data are generally more informative, contain

[1] Opioids include natural opioids such as morphine and codeine, semisynthetic opioids such as oxycodone, hydrocodone, hydromorphone and oxymorphone, and synthetic opioids such as methadone, tramadole and fentanyl. Heroine is an illicit opioid synthesized from morphine. Prescription opioids include natural and semisynthetic opioids and methadone (Scholl et al. 2019).

[2] This is well documented in Rossen et al. (2014), Buchanich et al. (2016) and Stewart et al. (2016) among others.

more degrees of freedom and less multicollinearity between variables than cross-sectional data, and improve the efficiency of econometric estimates (see Elhorst 2021). Panel data contain information on both the intertemporal dynamics and the individuality of the observational units (regions), and allow one to control the effects of missing and unobserved variables (for more details, see Hsiao 2007).

The objective of our study is to employ a spatial Durbin panel data model, an extension of the cross-sectional model to a panel data framework, for estimating direct and indirect (cross-state spillovers) effects of a set of key factors that influence state-level patterns of opioid mortality. Specifically, we consider five variables to capture the racial/ethnic structure of a state, four variables to cover the state's age structure and two variables to represent the educational attainment level of its population. We also include three covariates that address economic distress: the poverty rate, the unemployment rate and the lower income variable. In addition, the opioid prescription rate is used to account for one of the opioid supply factors to US mortality rates.

The model is applied to 49 states over six years from 2014 to 2019. A k-nearest-neighbor matrix is chosen to represent the topological structure between the states.[3] Calculation of effects estimates is based on Bayesian estimation and inference, and reflects a proper interpretation of the marginal effects for our nonlinear model that involves lags of the dependent variable vector. The study provides a rich picture on how determinants affect opioid mortality. The findings clearly point to the important role indirect (spillover) effects play. A neglection of the spillover effects would cause incorrect inferences.

The remainder of the paper is structured as follows. Section 2 presents the econometric framework, outlines the proposed model, discusses prior selection for Bayesian estimation of the model, and shows how to calculate direct and indirect effects estimates necessary for proper interpretation of the model estimates. Section 3 outlines model specification issues, provides a brief summary of the data set used, and then presents the direct and indirect effects estimates of the explanatory variables on the opioid mortality rates. The last section summarises and concludes the paper.

[3]This weight matrix constrains the neighbor structure to the k-nearest neighbors. For a definition of k-nearest neighbor matrices see, for example, Fischer and Wang (2011)

2 Econometric Framework

2.1 The model

The econometric approach we employ in this study is a spatial econometric panel data model that is known as spatial Durbin panel data model in the spatial econometrics literature (see, e.g., LeSage 2014) and can be written in matrix form as

$$y = \rho W y + X\beta + WX\theta + \iota_T \otimes \mu + \nu \otimes \iota_N + \epsilon \tag{1}$$

where y is the $NT \times 1$ dependent variable vector of opioid mortality rates in state i ($i = 1, ..., N$) at time t ($t = 1, ..., T$), organized with t being the slow index for elements y_{it} in the vector y. X is an $NT \times Q$ matrix of Q explanatory variables that is organized in the same way. β is the associated $Q \times 1$ parameter vector.

W is an $NT \times NT$ weight matrix that represents connections between the states and has a block diagonal form: $I_T \otimes w$, with $\otimes$ being a Kronecker product. w is a $N \times N$ spatial weight matrix reflecting spatial proximity of the N states that make up the panel of states over $t = 1, ..., T$ time periods. The diagonal elements $w_{ii} = 0$ ($i = 1, ..., N$), and the matrix is row-normalized to have row-sums of unity. The $NT \times 1$ matrix-vector product Wy is referred to as spatial lag and reflects a linear combination of neighboring state values for the dependent variable. The scalar parameter ρ denotes the spatial dependence parameter that indicates the strength of spatial dependence between the vector y and the vector Wy.[4] The $NT \times Q$ matrix-matrix product WX is used to create spatial lags of the Q explanatory variables of the model, and represents a linear combination of characteristics from neighboring states, with the associated parameters θ.

$\iota_T \otimes \mu$ represents an N-vector of state-specific fixed effects μ, with $\otimes$ being a Kronecker product that repeats the vector μ for each time period. $\nu \otimes \iota_N$ reflects a Kronecker product of the T-vector of time-specific effects ν, one for each time period. The $NT \times 1$ vector ϵ is a stochastic disturbance

[4]Note that the dependence parameter ρ is well defined over a limited interval that safeguards the existence of the matrix inverse $R^{-1} = (I_{NT} - \rho W)^{-1}$. This interval is $(\lambda_{min}, \lambda_{max})$, where λ_{min}, λ_{max} are the minimum and maximum eigenvalues of the matrix $(I_{NT} - \rho W)$, respectively (LeSage 2021). λ_{min} will be negative, and λ_{max} will be one, provided the matrix W is row-normalized. In this study we use a lower bound of -1 to avoid the need to calculate the minimum and maximum eigenvalues of the large matrix R.

term, assumed to be normally distributed with zero mean and a scalar variance, σ^2.

$$\epsilon \sim \mathcal{N}(0_{NT}, \sigma^2 I_{NT}) \tag{2}$$

2.2 Bayesian estimation

Estimation of the spatial Durban panel data model outlined in Eq.(1) is based on Markov Chain Monte Carlo (MCMC) estimation, with prior distributions assigned to the parameters ρ, $\delta = (\beta, \theta)'$ and σ^2 (see Mills and Parent 2021 for a recent survey of Bayesian inference methods in regional science).[5] Parameter restrictions are imposed on the dependence parameter ρ during MCMC sampling, using methods described in LeSage (2020), and LeSage and Fischer (2020). MCMC estimation involves sequentially sampling each parameter from their conditional distributions. One of the main advantages of MCMC sampling is that conditional distributions for each parameter, given values of all other model parameters, take a form that is computationally simple to sample from (LeSage 2020).

The prior setup we use is standard. We rely on a normal prior for the parameters $\delta = (\beta, \theta)'$, associated with the X- and WX-variables, as in LeSage and Fischer (2020):

$$p(\delta) \sim \mathcal{N}(\bar{\delta}, \bar{\Sigma}_\delta) \tag{3}$$

where $\bar{\delta}$ is a $2Q \times 1$ vector of prior means, and $\bar{\Sigma}_\delta$ a $(2Q) \times (2Q)$ prior variance-covariance matrix. We set the prior means to a value of 0.5 and the prior variance to 0.001.

For the dependence parameter ρ we employ a uniform prior

$$p(\rho) \sim U(-1, 1) \tag{4}$$

because this scalar parameter is constrained to lie in the open interval $(-1, 1)$. The constraint is imposed during MCMC estimation using a Metropolis-Hastings approach with rejection sampling, using methods described in LeSage and Fischer (2020), and LeSage (2020).

An informative prior is placed on the noise variance parameter σ^2, because we use an inverse

[5] For μ and ν no priors, just demeaning transformations are used (see LeSage 2021).

gamma $(\bar{a}, \bar{b})$ distribution shown in Eq. (5).

$$p(\sigma^2) = \frac{\bar{b}^{\bar{a}}}{gamma(\bar{a})} \ (\sigma^2)^{-(\bar{a}+1)} \ exp(-\bar{b}/\sigma^2) \tag{5}$$

where $\bar{a} \rightarrow 0$, $\bar{b} \rightarrow 0$ reflect no prior information for this parameter.

As is traditional in the literature, we assume that priors for ρ, δ and σ^2 are independent. Given these priors we use the conditional distributions described in LeSage and Fischer (2020). A set of 4,000 draws were taken for determining posterior estimates of the parameters, with the first 500 omitted for burn-in of the sampler.

2.3 Direct and indirect impact estimates

The estimates for the coefficients β and θ, unfortunately, are not meaningful as LeSage and Pace (2009) point out, if one is interested how changes in the explanatory variables impact the dependent variable outcome, which is the object of interest in this paper.[6] We follow the suggestion of LeSage and Pace (2009) to calculate direct and indirect effects estimates that reflect a proper interpretation of the marginal effects for our nonlinear model that involves spatial lags of the dependent variable.[7]

The partial derivatives used to calculate the direct and indirect effects estimates take the form of an $NT \times NT$ matrix. Using matrix notation, the partial derivative for the qth explanatory variable X^q can be written as shown in Eq. (6).

$$\partial y / \partial X^q = (I_{NT} - \hat{\rho} W)^{-1} \ (\hat{\beta} + W\hat{\theta}) \tag{6}$$

where $\hat{\rho}, \hat{\beta}$ and $\hat{\theta}$ denote parameter estimates. Diagonal elements of this matrix represent own-partial derivatives, while off-diagonal elements reflect cross-partial derivatives.

Using the mean of the main diagonal elements of the matrix of partial derivatives in Eq. (6) produces a scalar summary of the *direct effects*. Direct effects show how changes in the qth explanatory

[6] One implication of the nonlinear relationship between y and X in our model is that changes in the qth variable $(q = 1, ..., Q)$ for a single observation i can potentially impact all observations in the dependent vector y.

[7] See LeSage and Pace (2021) for a discussion of issues surrounding proper interpretation of the estimates from a variety of spatial regression models.

variable for the ith state impact the ith state's dependent variable for $i = 1, ..., N$. Using the mean of these NT different values generates a scalar summary that may be interpreted as representing how a change in the qth explanatory variable in the typical state impacts outcome y for the typical state (LeSage and Pace 2021).[8]

Indirect effects represent the impact of the ith state outcomes y_i from a change in the qth explanatory variable from the jth state, and capture the off-diagonal elements of the $NT \times NT$ matrix. Specifically, the elements in the ith row of the matrix show

$$\partial y_i / \partial X_j^q \text{ for } i \neq j; \; i = 1, ..., N$$

reflecting how changes in each of the other states' qth explanatory variable impact outcomes in the jth state. LeSage and Pace (2009) suggest using the mean of the sum of the off-diagonal elements from each row to produce a scalar summary measure of *cumulative indirect effects* or *spatial spillovers*.

Note that our model can have positive (or negative) direct effects associated with negative (or positive) indirect effects for the qth variable, so that spillover impacts might work in the opposite direction of direct impacts, arising from changes in each explanatory variable. *Total effects* represent the sum of direct and indirect effects. In addition to calculating scalar summary measures of the effects, there is a need to calculate an empirical distribution from which measures of dispersion for the effects can be constructed and used for inference regarding the statistical significance of the effects (LeSage and Pace 2021). This is done using a sequence of say 1,000 MCMC draws for the parameters ρ, β, θ to calculate a sequence of 1,000 scalar summary measures of these effects that reflect the posterior distributions.

Given an estimate of the standard deviation for the scalar summary point estimates we can test hypotheses regarding the significance of the various types of effects for each of the explanatory variables used in the model. t-statistics, t-probabilities, and lower 0.05 and upper 0.95 credible intervals can be computed using the retained MCMC draws. The mean of the draws for direct

[8]Since the panel model includes time-specific fixed effects that capture variation over time periods, we can reasonably average the scalar summary estimates. But these scalar summary measures might ignore impact information over all time periods regarding the impact of changing values X^q at the observation level of direct (indirect) effects of the N states.

effects (for each of the Q explanatory variables), for example, and the standard deviation of the draws is taken to construct the t-statistic, which is then used to find the associated t-probability. The lower 0.05 and upper 0.95 are based on the MCMC draws. Given a set of 1,000 MCMC draws, the lower 0.05 interval would be determined by the 50th value from the lowest set of sorted values, and the upper 0.95 by the 950th value from this sorted set (LeSage 2021).

3 Application of the Model

This section applies the model. The empirical model estimated uses a pool of the 49 contiguous US states ($N = 49$) over six years from 2014 to 2019 ($T = 6$). The dependent variable vector y represents the annual opioid mortality rates and we consider a suit of Q=17 explanatory variables. The choice of the time was based on the availability of data.

3.1 Model specification issues

The definition of a spatial lag in spatial regression models in general and our spatial Durbin panel data model in particular depends on the choice of a spatial weight matrix that summarizes the topology of the data set. Clearly, a large number of weight matrices can be derived for the same spatial layout (see Fischer and Wang 2011 for a review). In this study we use a nearest-neighbor-based weight matrix that constrains the neighbor structure to the k-nearest neighbors. The number of neighbors, k, is the parameter of this weighting scheme. Its choice is an empirical issue (see LeSage and Fischer 2008) yielding k=8 neighbors in this study.[9]

W is an 234×234 weight matrix that represents connections between the states and has a block diagonal $I_T \otimes w$, with $\otimes$ being a Kronecker product. w is a 39×39 spatial weight matrix constructed based on 8-nearest neighboring states and identical during each time period in our model formulation. The diagonal elements $w_{ii} = 0$ $(i = 1, ..., 39)$, and the matrix is row-normalized to have row-sums of unity. The 234×1 matrix-vector product Wy is referred to as spatial lag and reflects a linear-combination of neighboring states values for the dependent variable vector of

[9]Comparing ten different k-neighbor matrices running from k=1 to k=10, we find that k=8 leads to a log-marginal likelihood of -174.8609 and an associated model probability of 0.9999, close to one.

opioid death rates. The $234 \times Q$ matrix product WX is used to create spatial lags of the $Q = 17$ explanatory variables described in the following subsection.

3.2 Data and data sources

Data for the dependent variable vector y come from the US Centers for Disease Control and Prevention (CDC) Wonder Online Databases of Multiple Cause of Death, filtered for drug-related causes of death including opioids, synthetic opioids and psychostimulants, estimated per 10,000 population for each state and year.[10] Our opioid mortality rates capture all opioids including fentanyl that is the prime cause of death now. Based on prior research we selected the following set of X-variables to explain variation in state-level mortality rates over the observation period.[11]

(a) Five variables are considered to capture the racial/ethnic structure of a state: the percentage of the population who identify as *White*, *Black or African American*, *American Indian and Alaska Native*(=*Native Americans*), *Asian*, *Hispanic or Latino* races. The data were derived from the US Census Bureau's Population Estimates Program called American Community Survey (ACS).

(b) To uncover the impact of age on mortality rates we include age in five categories: the percentage of people with *18-24 years*, *25-34 years*, *35-44 years*, *45-64 years*, and *65 years and more* (Data source: ACS).

(c) The level of educational attainment is widely viewed as a relevant factor affecting opioid mortalities (see, for example, Blake-Gonzalez et al. 2021). Educational attainment is measured in terms of two variables, the percentage of people who hold a *high school's degree or higher* and the percentage of people having a *bachelor's degree or higher* in each state every year (Data source: ACS).

[10]The Multiple Cause of death data are county-level national mortality and population data. The data are based on death certificates for US residents. Each death certificate contains a single underlying cause of death and up to twenty additional multiple causes. Note that more than 80 percent of drug overdose death certificates named at least one drug in 2017 and 2018. Drug-specific overdose numbers and rates might have changed substantially from 2017 to 2018 as a result of changes in reporting in some states (see Wilson et al. 2020).

[11]For the rationale choosing these variables, see Sun (2022), Blake-Gonzalez et al (2021), Wilson et al. (2020), Bohnert et al. (2019), Marotta et al. (2019), Nechuta et al. (2018) and King et al. (2014) among others.

(d) Economic conditions could account for up to one-tenth of the rise of drug and opioid mortality rates (Blake-Gonzalez et al. 2021). Following Nosrati et al. (2019) we consider three variables that address economic distress: the *poverty rate*, the *unemployment rate* and the variable *lower income* in each state and year. The *poverty rate* is calculated as the percentage of population whose income falls below the state-specific level per year, while *lower income* is measured in terms of the number of people with income of less than $ 34,999 per 10,000 persons . The *unemployment rate* is given as percentage of people aged 16 years and older who are in the resident labor force, but unemployed. The data for these variables come from ACS.

(e) The next variable relates to one of the opioid supply factors to US opioid mortality rates, measured in terms of the *opioid prescription rate* per 100 person in each state every year.[12] The prescription rates for opioids vary widely across states, with Alabama and Arkansas having the highest rates in 2018. The data come from the US Opioid Dispensing Rate Maps provided by IQVIA Xponent from the CDC in 2020. The prescription rate is calculated by dividing the total number of opioid prescriptions dispensed annually by annual resident population and multiplying the number by 100.

(f) The final explanatory used in this study is health insurance coverage, measured in terms of the percentage of people with *health insurance* in each state and year (Data source: ACS).

3.3 Estimation results and interpretation of the coefficient estimates

This subsection presents the estimation results of the model and quantifies the impact of the explanatory variables on the opioid mortality rates, using the scalar summary direct and indirect impact measures described in Section 2.3.

[12]The recent spike in the number of opioid deaths has been reported widely and linked to the expanded use of prescription opioids and potentially inappropriate opioid prescribing practices (see Stewart et al. 2017 and Stopka et al. 2019).

Table 1: Posterior parameter estimates of the spatial Durbin panel data model

Variable (Parameter)	Posterior Mean	Asymp. t-stat	z-prob.
Percent White (β_1)	-0.0163*	-0.7389	0.4600
Percent Black/African American (β_2)	0.0078*	0.1706	0.8645
Percent Native (β_3)	-0.2221*	-1.8458	0.0649
Percent Asian (β_4)	-0.2059	-2.3068	0.0211
Percent Hispanic/Latino (β_5)	0.0360*	0.7658	0.4438
Percent Age 18-24 (β_6)	-0.1057*	-1.2978	0.1944
Percent Age 25-34 (β_7)	0.1372*	1.4731	0.1407
Percent Age 35-44 (β_8)	0.0610*	0.5755	0.5650
Percent Age 45-64 (β_9)	-0.0594*	-0.8160	0.4145
Percent Age $\geq$ 65 (β_{10})	-0.1694	-2.2128	0.0269
Percent High School and above (β_{11})	-0.0807	-2.4654	0.0137
Percent Bachelor and higher (β_{12})	0.0466*	1.6510	0.0987
Poverty Rate (β_{13})	-0.0282*	-1.9677	0.0491
Lower Income(β_{14})	0.0238*	1.3788	0.1680
Unemployment Rate (β_{15})	0.0210*	0.6234	0.5330
Opioid Prescription Rate (β_{16})	-0.0064	-2.3763	0.0175
Percent Health Insurance (β_{17})	-0.0145*	-1.6671	0.0955
$W*$ Percent White (θ_1)	0.2098	2.5127	0.0120
$W*$ Percent Black/African American (θ_2)	-0.3091*	-1.8291	0.0674
$W*$ Percent Native (θ_3)	-0.7714*	-1.7840	0.0744
$W*$ Percent Asian (θ_4)	0.7766	2.4292	0.0151
$W*$ Percent Hispanic/Latino (θ_5)	0.6277	3.1032	0.0019
$W*$ Percent Age 18-24 (θ_6)	0.0487*	0.2115	0.8325
$W*$ Percent Age 25-34 (θ_7)	-0.3329*	-1.1208	0.2624
$W*$ Percent Age 35-44 (θ_8)	-0.7836	-2.9728	0.0030
$W*$ Percent Age 45-64 (θ_9)	-0.2515*	-1.0777	0.2812
$W*$ Percent Age $\geq$ 65 (θ_{10})	-0.8490	-4.7356	0.0000
$W*$ Percent High School and above (θ_{11})	-0.0220*	-0.2096	0.8340
$W*$ Percent Bachelor and higher (θ_{12})	0.0962*	1.0993	0.2716
$W*$ Poverty Rate (θ_{13})	-0.1078	-2.1844	0.0289
$W*$ Lower Income (θ_{14})	0.1852	3.7613	0.0002
$W*$ Unemployment Rate (θ_{15})	-0.4948	-5.7702	0.0000
$W*$ Opioid Prescription Rate (θ_{16})	-0.0222	-2.5986	0.0094
$W*$ Percent Health Insurance (θ_{17})	-0.0158*	-0.9359	0.3493
Rho (ρ)	0.2939	4.0535	0.0001

Notes: Results are based on a k-nearest neighbor matrix W with $k = 8$ nearest neighboring states; $N = 39$, $T = 6$ and $Q = 17$; parameter estimates calculated using LeSage's (2021) Panel Data Toolbox for MATLAB; performance: log-marginal likelihood= -174.8609, R-square= 0.9353, corr-square= 0.6507 and sigma-square= 0.0502; * indicates not significantly from zero

In Table 1 we report the posterior parameter estimates for the spatial Durbin panel data model, although these are not directly interpretable in terms of the impacts associated with changes in the X- and WX-variables on the dependent variable. The table also summarizes the associated (asymptotic) t-statistics and the z-probabilities. t-statistics represent the posterior mean divided by the posterior standard deviation both of which are calculated from the retained MCMC draws. The t-statistics are then used to determine the associated z-probabilities. The table indicates and this is important to note that the parameter estimate of the spatial autoregressive parameter is positive ($\hat{\rho} = 0.2939$) and significantly different from zero, providing evidence for the existence of significant spatial effects working through the dependent variable.

The proper way to interpret the model results is in terms of the (summary) direct and indirect effects estimates of the X- and WX-variables. Table 2 outlines these cumulative effects estimates, along with inferential statistics. A positive (negative) mean with positive (negative) lower and upper credible intervals should be interpreted as a positive (negative) effect. Effects whose credible intervals span zero are not significant. The scalar summary effects estimates average over all the US states in the sample.[13]

Direct (own state) effects responses in Table 2 indicate five negative and significant effects. The own-state (direct) impact of changes in the percentage of the senior population (*65 years and older*) on the opioid mortality rate is negative (-0.2042) and significant at the 99 percent level. This result matches our intuition, as we should expect that a larger percentage of senior people in the typical state i would reduce the opioid mortality rate. The direct effect of *Native Americans* is negative (-0.2545) and significant at the 95 percent level while that of the *population with a high school degree or higher* (-0.0825), the *poverty rate* (-0.0327) and the *opioid prescription rate* (-0.0073) are also negative and significant, but at a much lower magnitude. The variables *percent Hispanic/Latino*, *percent age 25-34* and *percent age 35-44* are positive, but not significantly different from zero. All other estimates reported in Table 2 are negative, but not significantly different from zero.

[13]Relying on the scalar summary effects estimates might obscure important variation over time in the direct and indirect effects that may be of substantive interest in spatial regression relationships being analysed. In such cases plots of the observation-level direct and indirect effects should be considered.

Table 2: Direct and indirect impact estimates for changes in X- and WX-variables

Impact Estimates	Posterior Mean	t-stat.	t-prob.	Lower 0.05	Upper 0.95
Direct Impact Estimates					
Percent White	−0.0085*	−0.3738	0.7087	−0.0524	0.0353
Percent Black/African American	−0.0041*	−0.0842	0.9330	−0.1000	0.0873
Percent Native	−0.2545	−2.0072	0.0453	−0.5028	−0.0083
Percent Asian	−0.1785*	−1.9235	0.0550	−0.3623	0.0016
Percent Hispanic/Latino	0.0606*	1.2011	0.2303	−0.0356	0.1582
Percent Age 18-24	−0.1050*	−1.2992	0.1945	−0.2639	0.0500
Percent Age 25-34	0.1262*	1.3160	0.1888	−0.0583	0.3103
Percent Age 35-44	0.0316*	0.2972	0.7664	−0.1774	0.2446
Percent Age 45-64	−0.0698*	−0.9563	0.3394	−0.2075	0.0750
Percent Age ≥65	−0.2042	−2.6293	0.0088	−0.3535	−0.0522
Percent High School and above	−0.0825	−2.4486	0.0147	−0.1488	−0.0167
Percent Bachelor and higher	0.0508*	1.7462	0.0814	−0.0075	0.1085
Poverty Rate	−0.0327	−2.2147	0.0272	−0.0610	−0.0037
Lower Income	0.0312*	1.7802	0.0757	−0.0025	0.0672
Unemployment Rate	0.0021*	0.0630	0.9498	−0.0654	0.0688
Opioid Prescription Rate	−0.0073	−2.6367	0.0086	−0.0127	−0.0018
Percent Health Insurance	−0.0153*	−1.7790	0.0759	−0.0321	0.0012
Indirect Impact Estimates					
Percent White	0.2851	2.3991	0.0168	0.0569	0.5318
Percent Black/African American	−0.4279*	−1.7446	0.0817	−0.9173	0.0489
Percent Native	−1.1673*	−1.8483	0.0652	−2.4187	0.0171
Percent Asian	0.9952	2.1655	0.0308	0.1122	1.9368
Percent Hispanic/Latino	0.8889	2.9519	0.0033	0.3175	1.5079
Percent Age 18-24	0.0244*	0.0776	0.9382	−0.5871	0.6369
Percent Age 25-34	−0.4046*	−0.9602	0.3374	−1.2489	0.4292
Percent Age 35-44	−1.0646	−2.8531	0.0045	−1.8139	−0.3602
Percent Age 45-64	−0.3749*	−1.1445	0.2530	−1.0468	0.2564
Percent Age ≥65	−1.2530	−4.4361	0.0000	−1.8542	−0.7393
Percent High School and above	−0.0640*	−0.4300	0.6674	−0.3648	0.2361
Percent Bachelor and higher	0.1535*	1.2188	0.2235	−0.0835	0.4039
Poverty Rate	−0.1619	−2.2505	0.0249	−0.3084	−0.0266
Lower Income	0.2680	3.5939	0.0004	0.1306	0.4227
Unemployment Rate	−0.6805	−5.0752	0.0000	−0.9641	−0.4371
Opioid Prescription Rate	−0.0336	−2.6377	0.0086	−0.0594	−0.0097
Percent Health Insurance	−0.0280*	−1.2301	0.2193	−0.0754	0.0158

Notes: Impact estimates are calculated using LeSage's (2021) Panel Data Toolbox; * indicates not significantly different from zero.

The impact estimates differ from the corresponding coefficient estimates outlined in Table 1. The difference is due to some feedback effect that comes into play in the direct effects estimates. The discrepancy is positive since the impact estimates exceed the coefficients, reflecting some positive feedback. Note that it would be a mistake to interpret the β-parameters as representing direct effects estimates. If we would incorrectly view, for example, the model coefficient β_3 on the *percent Native American* variable as representing the direct impact, this would lead to an effect not significantly different from zero. But the true direct impact estimate points to effects estimates that are negative and significant.

Table 2 also shows the cumulative indirect (cross-state spatial spillover) effects with a change in the WX-variables. The indirect impact of the percentage of the senior population (*65 years and older*) in neighboring states j ($j \neq i$) is negative and significant at the 99 percent level. The cumulative spillover magnitude of 1.2530 appears to be rather large when compared to the direct effects magnitude of 0.2042. It must be noted, however, that the indirect impact estimates are cumulative spillovers where cumulation takes place over all neighboring states $j \neq i$, neighbors to the neighboring states, and so on. While this may seem counterintuitive, the indirect effects falling on any single state would be generally much smaller, consistent with spillovers being a "second-order effect". Also, the largest indirect effects would fall on nearby states. It is the cumulation of the spatial spillovers over all states that leads to relatively larger indirect than direct effects. Of course, one could investigate direct and indirect impacts for an individual state without averaging, but this would take the form of a 1-by-294 row vector for each state.

Moreover, it is worth noting that the indirect (spatial spillover) impact of the percentage of the age group *35-44 years* in neighboring states j ($j \neq i$) is negative (-1.0646) and significant at the 99 percent level, while the indirect impact estimates of the percentages of *Asian*, *Hispanic/Latino* and *White* populations in neighboring states j are significant and positive: 0.9952, 0.8889 and 0.2851, respectively. Finally, the following variables exert significant indirect effects on opioid mortality rates: the *opioid prescription rate* (-0.0336), the *poverty rate* (-0.1619), *lower income* (0.2680), and the *unemployment rate* (-0.06805). These results provide empirical evidence for cross-state spillover effects and highlight that the features of neighboring states are important determinants of mortality.

4 Closing Remarks

This paper shows that the spatial Durbin panel data model is a suitable model specification for quantifying the direct and indirect impact of a suit of explanatory variables on opioid mortality rates in a panel data framework. The analysis provides evidence for the existence of spatial externalities and interaction. Since the model involves spatial lags of dependent and independent variables, the traditional least-squares ceteris paribus interpretation of the regression parameters does not hold any longer. Thus, direct and indirect (spillover) effects estimates had to be calculated to quantify the impact of the explanatory variables on the variable vector that represents the state-specific opioid mortality rates over 2014 to 2019.

The main results of the analysis may be summarized in terms of the total effects estimates as follows.[14] *First*, *opioid prescription* has a negative total effect, statistically different from zero but with a rather low magnitude of 0.0409. *Second*, more important are the *race/ethnicity* categories. The *Hispanic/Latino*, but also the *White American* category reveals a statistically significant positive total impact effect (0.9495 and 0.2766, respectively) while the impact of *Native Americans* is negative (-1.4218) and significant. *Third*, *age* plays the most important role evidenced by a total effects estimate of -1.4572 in the case of the senior population (*65 years and older*) and -1.0330 in the case of the age category *35-44 years*, both are highly significant. *Fourth*, the total impacts of the *poverty rate* (-0.1946), the *unemployment rate*(-0.6784) and the *lower income* variable (0.2992) − that capture economic despair on the drug overdose death rates − are significantly different from zero and much more important than the *opioid prescription rate* (0.0409). A *final* point to note is the important role that spillover effects play whose omission would lead to incorrect inferences. Space matters and may lead to a better understanding of why and how neighboring states contribute to the opioid-induced mortality in the typical US state.

The study provides a rich picture on how potential determinants affect opioid mortality in US states, yielding useful insights to motivate the adoption of regional public policies for tackling the opioid crisis. State-specific policies may be derived by calculating observation-level direct and

[14]Note that total impact estimates are defined as sum of the direct and indirect estimates, but inference statistics has to based on the sum of the two coefficients $\hat{\beta} + \hat{\theta}$, and a proper measure for dispersion of this sum of coefficients. This can be constructed from the MCMC draws.

indirect effects. This, however, would require to analyse 294x1 row vectors, one for each of the 49 states, and this might be done in future studies.

Note that all the inferences were made conditional on the data and the specification of the spatial weight matrix. The assumption that a particular spatial weight specification is correct might be relaxed by explicitly incorporating model uncertainty in the statistical analysis. To accommodate this uncertainty issue one might use a convex combination of spatial weight matrices to be used for estimation of the model, in the spirit of Fischer and LeSage (2020).

Our future work in this area will expand into county-level opioid mortality to identify specific factors leading to premature deaths. We will be using more demographic variables to design an early warning system to assist in public health communication.

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