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A NEW PROPOSAL TO ADJUST MORAN'S *I* FOR POPULATION DENSITY

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SUMMARY

We analyse the effect of using prevalence rates based on populations with different sizes in the power of spatial independence tests. We compare the well known spatial correlation Moran's index to three indexes obtained after adjusting for population density, one proposed by Oden, another proposed by Waldhör, and a third proposed by us in this paper. We find an effect of spatially correlated populations in the type I error probability on the test based on Moran's and Waldhör's indexes. We conclude also that the test proposed by Oden is powerful to test risk heterogeneity, but it has disadvantages when the interest is solely on the spatial correlation of morbidity risks. In this latter case, we recommend using our proposed test which is more powerful than the usual Moran's index applied directly to the rates. Copyright © 1999 John Wiley & Sons, Ltd.

1. INTRODUCTION

In epidemiological studies it is frequently of interest to know whether the occurrence rate of a certain event is spatially correlated in a given area. Usually, one tests whether rates of geographically contiguous areas are more similar or more dissimilar than expected under the hypothesis that risk distribution is unrelated to the spatial location of the areas. The similarity degree is usually measured through spatial autocorrelation indexes, the most popular being Moran's index, denoted by I (see Moran[1]) with distributional properties studied by Cliff and Ord.[2] Examples of applications of the indexes to disease distribution studies include Able and Becker,[3] Ohno *et al.*,[4] Grimson *et al.*[5] and Kemp *et al.*[6] Recently, Jacqmin-Gadda *et al.*[7] proposed an adjustment to Moran's I for covariate effects.

Consider a region divided in m areas and let n_i and x_i be the number of cases and the risk population in area i, respectively, with $i = 1, \ldots, m$. The observed rate in area i is defined as $p_i = n_i/x_i$. Moran's I is given by

$$I = \frac{m}{\sum_{ij} w_{ij}} \frac{\sum_{ij} w_{ij}(p_i - \bar{p})(p_j - \bar{p})}{\sum_i (p_i - \bar{p})^2} \tag{1}$$

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where the value w_{ij} is the weight assigned to areas i and j, and $\bar{p} = \sum_i p_i/m$. Usually, w_{ij} will reflect the geographical distance between areas i and j, being defined, for example, as $w_{ij} = 1$ if $i \neq j$ and the areas are adjacent, and by $w_{ij} = 0$, otherwise. However, weights can be more general depending, for example, on functions of distances between areas (for example, Whittemore *et al.*[8] and Tango[9]). Moran's I usually ranges between -1 and 1, with large positive values indicating neighbourhood similarity of the rates and values close to zero indicating absence of spatial autocorrelation.

The null hypothesis probability distribution of Moran's I has been calculated under two different assumptions. The first assumes that the rates are independently and identically distributed (i.i.d.) random variables with a normal distribution. This implies that the expected value of the rates is constant in all areas which in turn seems to conflict with the common situation of unequal but spatially uncorrelated underlying rates.

A less restrictive assumption is used in association with a permutation test. In this case, the rates are considered random variables with an exchangeable distribution and the null distribution is obtained by calculating the empirical distribution of Moran's I resulting either from all or from a large sample of the permutations of the rates among the areas. Therefore, with the permutation approach, it can be tested if potentially different rates' distributions are spatially uncorrelated.

1.1. Effects of varying population sizes

In practice, however, both assumptions underlying Moran's I null distribution are violated. Consider, for example, a region partitioned on areas with different sized populations, such as a state and its counties. Hence, when estimating the underlying rate in each area through the observed prevalence or incidence rate (number of cases divided by the number of person-years at risk), we are using measures with different variances in the calculation of the indexes.

As Besag and Newell[10] pointed out, in the case of the permutation test it is assumed under the null hypothesis that any permutation of the observed p_i among the m areas is equally probable. However, when the populations are different, areas with small population have more variable rates and hence they are more likely to assume an extreme value. Additionally, since population density tends to display a spatial structure, so do the p_i.

Only recently did researchers start to study the effects of deviations from the i.i.d. or exchangeable case on the spatial autocorrelation tests. Walter[11, 12] shows that the probability of a type I error in tests based on some spatial autocorrelation measures is larger than the nominal value when the populations in the areas are heterogeneous and the underlying risk is constant. In his simulations, Walter does not find this effect in the test based on Moran's I. However, he does not study the effect of heterogeneous populations on the power of the test. That is, he does not evaluate the impact of population variation when there is spatial correlation between the underlying risks.

Oden[13] proposes a way to adjust Moran's I accounting for the differences among populations. His most powerful test statistic is defined as

$$I^*_{\text{pop}} = \frac{n^2 \sum_{ij} M^*_{ij}(e_i - d_i)(e_j - d_j) - n(1 - 2\bar{b}) \sum_i M^*_{ii} e_i - n\bar{b} \sum_{ii} M^*_{ii} d_i}{\bar{b}(1 - \bar{b})(x^2 \sum_{ij} d_i d_j M^*_{ij} - x \sum_i d_i M^*_{ii})} \tag{2}$$

where $n = \sum n_i$, $x = \sum x_i$, $\bar{b} = x/n$, $e_i = n_i/n$, $d_i = x_i/x$ and $M^*_{ij} = M_{ij}/\sqrt{(d_i d_j)}$. The value of M_{ij} can be interpreted as a spatial weight assigned to a pair of individual cases located in areas i and j. Generally, $M_{ii} \neq 0$.

In his simulations, Oden shows that his proposed test statistic is much more powerful than Moran's I when variation is present in the risk populations. He attributes the superiority of his index to its interpretation of variability of rates between areas as evidence of aggregation, even in the absence of spatial correlation. This capacity of capturing variability is due to the first term in the numerator which is a spatial version of the conventional chi-squared test for rates heterogeneity.

We consider inappropriate the comparison between Moran's I and I^*_{pop} presented by Oden[13] because the statistics are not testing the same pair of null and alternative hypothesis. Consider three states concerning the spatial configuration of the areas' risks:

A. spatially constant risk;
B. heterogeneous risks without spatial correlation;
C. heterogeneous risks with spatial correlation.

As we will show, Moran's I tests the null hypothesis $H_0: A \cup B$ against the alternative $H_1: C$ while Oden's statistics considers $H_0: A$ against $H_1: B \cup C$. Therefore, the tests disagree with respect to the status of B as a null hypothesis. It is not surprising therefore that I^*_{pop} has larger power especially at states like B, against which Moran's I should have at most power α, the type I error probability.

Waldhör[14] proposes another test to deal with the heteroscedasticity implied by different population sizes. He assumes that, under the null hypothesis, the rates p_i are independent and they have a normal distribution with a fixed mean but a variance σ_i^2 which differs between the areas. In the applications, he uses σ_i^2 inversely proportional to the population x_i. His test statistic is still Moran's I and its null distribution is assumed to be normal. Allowing for different σ_i^2, he then proposes a new estimate for the moments of I by applying theorems due to Pitman[15] and Koopmans.[16] The hypothesis of these theorems are invalid in this heteroscedastic situation but he proposes to apply them anyway, subsequently checking through simulations that the bias introduced is small. However, we show that, with a more realistic larger class of patterns, this last conclusion is not correct.

1.2. Objectives of the paper

We have three aims in this paper. The first is to re-evaluate the comparison between the tests based on Moran's I and those based on I^*_{pop} and Waldhör's I for the underlying risk and risk populations under a large variety of situations. We consider the influence of a number of possible factors on the probability of type I error and the tests' power. Three different structures for the areas' populations comprise this simulation: constant; variable without spatial correlation; and variable with spatial correlation. We also consider high and low risk level with spatial independence or spatial correlation.

In the course of the re-evaluation we show that Oden's I^*_{pop} and Waldhör I have disadvantages compared to Moran's I as tests for spatial autocorrelation even though they have very large power. In particular, Oden's great power seems to be concentrated on detecting heterogeneity of the rates, irrespective of spatial autocorrelation. This can be useful if the researcher is not interested in distinguishing between states B and C but, in general, it is more likely that the researcher would prefer to distinguish between them. In addition, we show that Waldhör's I tends to have type I error probability much larger than the nominal value when the population is not constant.

The second objective is to evaluate the effect of heterogeneous populations, with and without spatial structure, in the type I error probability and the power of Moran's I when using the heteroscedastic rates.

As a third objective, using an empirical Bayes approach, we propose a new test statistic which has larger power than Moran's I and does not present the shortcomings of Oden's I^*_{pop} or Waldhör's I.

The remainder of this paper is organized as follows: Section 2 deals with the first and second objectives described above while in Section 3 we introduce our proposal to adjust Moran's I. We present an example in Section 4 and in Section 5 we present our conclusions.

2. COMPARISON OF I^*_{pop}, WALDHÖR I, AND MORAN'S I

The simulation study to evaluate the behaviour of the tests is based on the spatial structure of the municipality of Belo Horizonte, in the state of Minas Gerais, Brazil. The total population in 1994 was 2,125,422 and was divided into 81 areas, called *planning units* (UP) (see Figure 1). The UP populations vary from 31 to 70,870 persons, with an average size of 26,240. First, second and third quartiles correspond to 9720, 26,140 and 40,480, respectively.

The neighbourhood structure of the UPs is kept constant in all simulations. For Moran's I, the weight w_{ij} is the adjacency indicator between areas i and j, with $w_{ii}=0$. For the index I^*_{pop}, we follow Oden[13] and set $M_{ij}=w_{ij}$ if $i \neq j$ and $M_{ii}=2$. In this way, the contribution to detect disease clustering of a pair of cases occurring in the same area is larger than that of a pair occurring in neighbouring areas. For Waldhör's I, we let $\text{var}(p_i)$ be inversely proportional to the population x_i.

The p-value of the test based on Moran's I is determined using 1000 permutations of the observed rates. The tests using I^*_{pop} and Waldhör's I are based on the normal approximation with mean and variance as given by Oden[13] and Waldhör.[14] The three tests are one-sided and they test against positive spatial autocorrelation, the most common case in practice.

In the simulations, the number of cases for the rates in each UP is generated according to the Poisson distribution with mean equal to the product of the population times the assumed risk of the UP. The UP population followed three structures:

(i) constant population size equal to 25,000, close to the actual average of Belo Horizonte UPs;
(ii) a pattern of area populations without spatial correlation. This pattern is obtained through a single permutation of the actual population sizes. The lack of spatial correlation is determined by Moran's I p-value of the generated pattern being equal to 0·18;
(iii) a spatially correlated population pattern given by the actual population distribution in the UPs which has Moran's I p-value equal to 0·02.

The simulated risk vector has a mean value θ at three levels representing a situation of low risk ($\theta=4{\cdot}75$ cases per 100,000 thousand inhabitants), another of high risk level ($\theta=4{\cdot}75$ cases per 1000 inhabitants), and an intermediate situation ($\theta=4{\cdot}75$ cases per 10,000 inhabitants).

The spatial structure of the risks is generated according to twelve situations, two of which have the condition of spatial independence. These two correspond to constant risk θ for all UPs and to risks generated by a log-normal distribution with mean θ and a coefficient of variation equal to 0·4. The remaining ten represent situations of increasing spatial correlation, with risks generated according to the simultaneous autoregressive model (SAR) (Whittle[17]). Denoting by Y the logarithm of the risk vector of the 81 UPs, the values of Y follow the model

$$Y=\eta+\rho G(Y-\eta)+\varepsilon$$

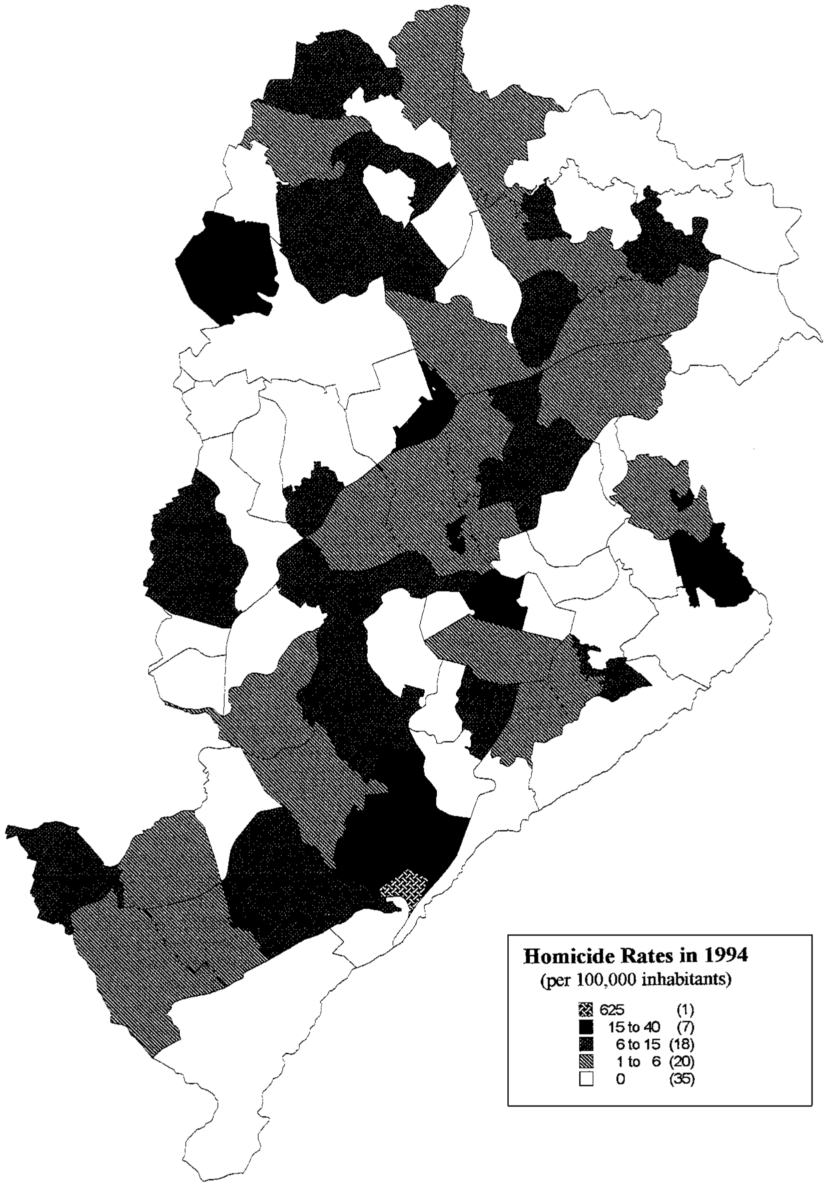

Figure 1. Map of homicide rates (per 100,000). Geographical units are the 81 planning units (UP) of Belo Horizonte, MG, Brazil, in 1994. The data were obtained from the Polícia Militar de Minas Gerais

where $0<\rho<1$ and ε is a vector with i.i.d. normal random variables with mean zero and variance σ^2. The logarithm of the risks has a mean equal to the vector η and covariance matrix $\sigma^2\,(I-\rho G)^{-1}\,((I-\rho G)^{-1})^{\mathrm{T}}$. The parameter ρ measures the degree of spatial association between the risks. The range of this correlation is given by the asymmetric matrix G, which is a matrix with

Table I. Type I error probability estimate (and 95 per cent confidence interval in parentheses) of one-sided tests ($\alpha = 0{\cdot}05$) based on 1000 simulations of constant risk or independently generated risks according to a log-normal distribution with mean θ and coefficient of variation equal to 0·4

Real risks	Constant population	Variable populations without spatial structure	Variable populations with spatial structure
Moran's I			
Constant $= \theta$			
$\theta = 4{\cdot}75/10^5$	4·1 (2·7; 5·5)	4·1 (2·7; 5·5)	5·5 (4·1; 6·9)
$\theta = 4{\cdot}75/10^4$	4·4 (3·0; 5·8)	2·9 (1·5; 4·3)	7·4 (6·0; 8·8)
$\theta = 4{\cdot}75/10^3$	5·3 (3·9; 6·7)	1·8 (0·4; 3·2)	7·7 (6·3; 9·1)
Log-normal, mean $= \theta$			
$\theta = 4{\cdot}75/10^5$	5·6 (4·2; 7·0)	3·8 (2·4; 5·2)	5·7 (4·3; 7·1)
$\theta = 4{\cdot}75/10^4$	4·5 (3·1; 5·9)	4·2 (2·8; 5·6)	6·2 (4·8; 7·6)
$\theta = 4{\cdot}75/10^3$	5·9 (4·5; 7·3)	4·0 (2·6; 5·4)	5·8 (4·4; 7·2)
Oden's I^*_{pop}			
Constant $= \theta$			
$\theta = 4{\cdot}75/10^5$	8·5 (7·1; 9·9)	8·1 (6·7; 9·5)	8·1 (6·7; 9·5)
$\theta = 4{\cdot}75/10^4$	9·7 (8·3; 11·1)	10·2 (8·8; 11·6)	8·6 (7·2; 10·0)
$\theta = 4{\cdot}75/10^3$	9·5 (8·1; 10·9)	10·6 (9·2; 12·0)	9·0 (7·6; 10·4)
Log-normal, mean $= \theta$			
$\theta = 4{\cdot}75/10^5$	15·4	15·2	16·3
$\theta = 4{\cdot}75/10^4$	91·1	91·4	91·5
$\theta = 4{\cdot}75/10^3$	100	100	100
Waldhör's test			
Constant $= \theta$			
$\theta = 4{\cdot}75/10^5$	5·0 (3·6; 6·4)	18·6	12·6
$\theta = 4{\cdot}75/10^4$	5·8 (4·4; 7·2)	16·0	11·7
$\theta = 4{\cdot}75/10^3$	4·4 (3·0; 5·8)	14·9	14·6
Log-normal, mean $= \theta$			
$\theta = 4{\cdot}75/10^5$	5·6 (4·2; 7·0)	17·1	15·9
$\theta = 4{\cdot}75/10^4$	5·4 (4·0; 6·8)	17·4	13·7
$\theta = 4{\cdot}75/10^3$	4·7 (3·3; 6·1)	23·3	14·4

normalized weights positive w_{ij}, summing 1 along the rows. In the simulations, we choose the parameters η and σ^2 such that $\exp(Y)$ is normally distributed with mean θ and coefficient of variation 0·4. The correlation parameter ρ assumes the values $0{\cdot}1, 0{\cdot}2, \ldots, 0{\cdot}9$ and 0·95.

2.1. Simulation results

The three tests present problems with respect to the type I error probability. Table I shows the proportion of significant results in 1000 simulations when tests are carried out with nominal significance level equal to 0·05. The tables express proportions multiplied by 100. The values in parentheses give a 95 per cent confidence interval for the actual type I error probability.

Moran's I is the least affected among the three tests. When the population is constant, the actual type I error probability is close to 5 per cent. However, it presents values different from the nominal value for variable populations such that it is smaller than nominal when populations are spatially independent and larger when populations are spatially correlated. However, the difference from the nominal value is at most 0·03.

We find much larger differences with the other two tests. Waldhör's I behaves well when the population is constant but it has error type I probability much larger than the nominal 0·05 when populations differ. It varies between approximately 15 per cent and 23 per cent when populations have no spatial structure and between 13 per cent and 15 per cent when they have spatial correlation. Hence, in contrast with the simulations in Waldhör,[14] we find a type I error uncontrolled at the nominal value. The reason for that is the different simulation scheme we adopted. In particular, it seems to matter considerably the fact that Waldhör[14] assumes a normal distribution for the rates, an implausible approximation in the case of most diseases.

The type I error probability of Oden's I^*_{pop} does not change much with the population pattern. When the risks are the same for all areas, irrespective of the population pattern, I^*_{pop} has a type I error probability almost twice as large as the nominal value. In the case of the heterogeneous but spatially uncorrelated risks, Oden's test is very powerful with its power increasing quickly as the risk level increases. Oden[13] sees this result as a good aspect of his test while we interpret it differently. Consider again the three states A, B and C of Section 1.1. Since Moran's I tests for spatial correlation, we have the pair of null hypotheses $H_0: A$ or B against the alternative $H_1: C$. Oden's statistics consider the pair $H_0: A$ against $H_1: B$ or C. Therefore, the tests are different with respect to the role of B, a pattern of heterogeneous but spatially independent risks; it is part of the null hypothesis for Moran's I but it is an alternative hypothesis for I^*_{pop}. This explains the type I error probability behaviour of Oden's test in this case.

Table II shows the power of the one-sided tests based on Moran's I, Waldhör's I and Oden's I^*_{pop} with nominal significance level 0·05. Each value is calculated with 500 simulations. Figure 2 displays the results for $\theta = 4{\cdot}75/10^4$, the intermediate risk situation, the other two situations being similar. Note that the vertical scales are not the same for all three plots.

We can observe in Table II that power decreases as the risk level decreases, probably because we tend to observe many areas with null rates making differentiation among their underlying rates more difficult. Incidentally, we note the drop in the power of all three tests when ρ increases from 0·9 to 0·95. This happens because an extremely high spatial autocorrelation generates very similar risks if the region is not large enough to allow for sufficient variation in the risks to appear.

When populations are heterogeneous, Moran's I power is approximately the same, irrespective of population spatial structure. However, we confirm the influence of the population heterogeneity on the test's power since it is smaller when the populations are variable. Compared to the case when population is constant, the heterogeneous population situation is about 50 per cent smaller unless the disease is very frequent, in which case the power is about 80 per cent smaller. In general, the power is moderately high if θ and ρ are not very small.

Waldhör's I is similar to Moran's I when the population is constant. Although the test statistic is the same on both tests in this case, Moran's I test is based on the permutation distribution while Waldhör's test is based on the normal approximation. Waldhör's test has larger power than Moran's I when the populations are heterogeneous or spatially structured. However, as we showed in Table I, part of this larger power is due to a larger than nominal type I error probability.

As we would expect from its motivation, I^*_{pop} does not have its power affected by the population heterogeneity. This test has very high power in the intermediate and high risk situations and higher power in the low risk situation than Moran's I and Oden's test.

Table II. Power estimate of one-sided tests ($\alpha = 0{\cdot}05$) based on 500 simulations of SAR generated risks with expected value θ, coefficient of variation equal to 0·4, and spatial correlation ρ. The risk population of the areas are chosen to be constant or different, with or without spatial correlation

Real risks	Constant population			Variable populations without spatial structure			Variable populations with spatial structure		
ρ	Moran's I	Oden's I^*_{pop}	Waldhör's test	Moran's I	Oden's I^*_{pop}	Waldhör's test	Moran's I	Oden's I^*_{pop}	Waldhör's test
$\theta = 4{\cdot}75/10^5$									
0·1	6·2	17·2	5·4	4·8	13·6	21·2	6·6	16·8	13·0
0·2	7·6	18·4	8·4	4·4	19·4	22·4	4·4	16·4	15·8
0·3	8·0	16·0	7·8	7·0	17·0	26·6	6·4	21·6	16·4
0·4	8·8	19·0	8·8	4·4	19·2	26·2	6·4	18·8	21·0
0·5	11·6	21·0	9·8	7·2	21·8	24·2	5·6	20·2	20·0
0·6	12·2	23·6	13·8	7·0	24·4	25·6	7·8	23·0	20·4
0·7	13·6	24·8	17·2	7·2	25·2	27·4	10·6	22·6	18·0
0·8	17·2	28·0	19·4	9·0	25·4	29·8	10·6	24·4	23·0
0·9	21·6	30·6	20·0	8·4	22·6	31·6	11·4	23·6	26·8
0·95	21·4	26·2	18·8	9·8	21·6	30·2	10·6	21·8	25·6
$\theta = 4{\cdot}75/10^4$									
0·1	9·0	94·6	11·4	4·8	94·2	23·4	6·2	92·8	15·6
0·2	13·0	95·2	12·0	5·8	95·6	30·2	8·6	94·0	21·0
0·3	20·0	96·4	21·8	12·4	95·2	30·8	8·6	96·2	20·6
0·4	33·8	98·2	40·4	12·2	98·0	42·2	15·6	96·6	28·8
0·5	47·4	98·0	47·4	19·2	98·2	46·6	24·6	97·0	34·2
0·6	61·8	97·0	67·8	22·4	98·8	53·4	26·8	98·0	40·4
0·7	71·8	98·2	79·4	28·2	98·4	58·4	36·8	98·0	48·8
0·8	83·4	98·2	88·4	39·6	97·8	66·0	38·4	98·2	56·0
0·9	87·2	95·2	88·4	43·0	98·6	63·6	44·2	95·8	55·6
0·95	82·8	89·4	78·8	39·4	90·6	64·2	34·6	89·0	51·8
$\theta = 4{\cdot}75/10^3$									
0·1	13·0	100	15·0	6·2	100	30·0	11·4	100	20·6
0·2	25·2	100	27·0	15·4	100	39·4	15·4	100	34·4
0·3	44·2	100	46·2	25·0	100	56·2	27·4	100	44·8
0·4	68·6	100	63·8	41·8	100	70·2	40·2	100	54·8
0·5	83·2	100	84·8	55·0	100	78·6	53·2	100	72·0
0·6	94·2	100	93·8	65·2	100	86·0	65·8	100	78·6
0·7	97·8	100	98·8	78·4	100	90·8	71·8	100	86·6
0·8	99·4	100	99·4	85·2	100	92·4	85·2	100	87·8
0·9	100	100	100	88·8	100	94·6	86·4	100	90·0
0·95	100	100	99·8	83·2	100	93·0	83·0	100	86·6

The comparison of Oden's power with the other two tests is not so obvious since they consider different null hypotheses. It is not clear how much of this power is due to the simple heterogeneity of the rates or to the spatial autocorrelation of the heterogeneous rates. In fact, in Table I we showed that, even under spatially independent risks, Oden's test often rejects H_o and this suggests that its power could not increase substantially with the increase of the spatial autocorrelation.

To address this issue, we ran additional simulations for Oden's and Moran's statistics where, for a fixed spatial correlation degree ρ, the variability of the risks is gradually increased (Figures 3(a)

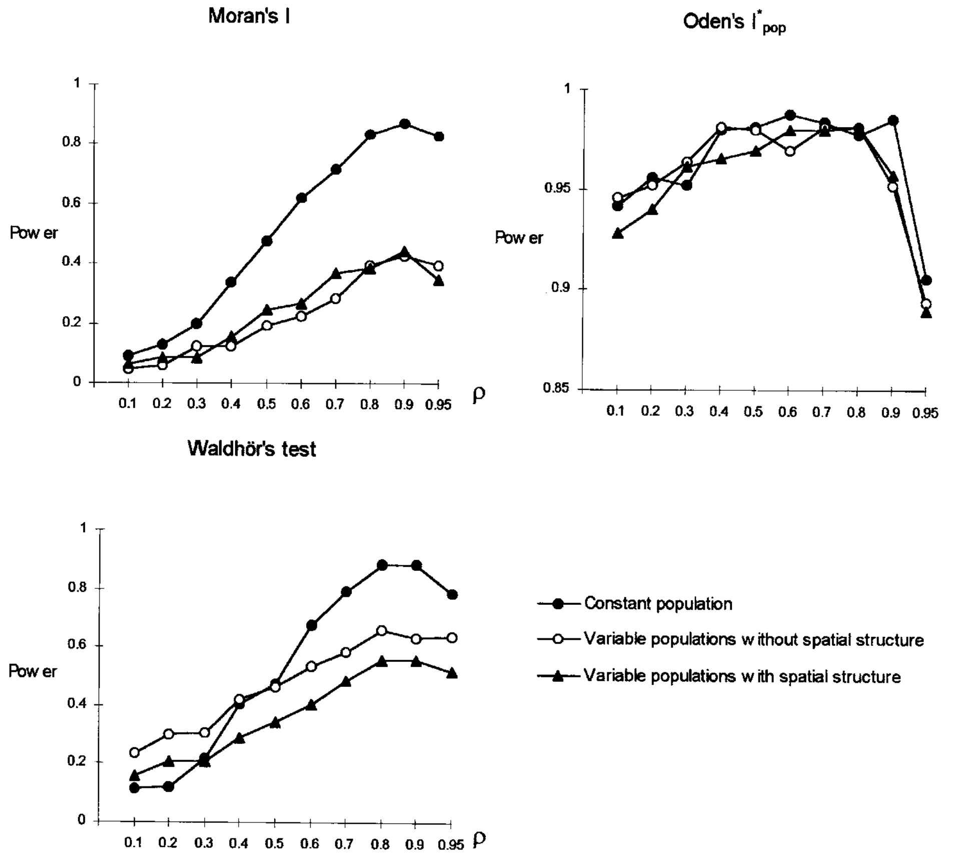

Figure 2. Power estimates of one-sided tests ($\alpha = 0{\cdot}05$) with Moran's I, Oden's I^*_{pop}, and Waldhör's I based on 500 simulations. The risks follow the SAR model with mean θ, parameter ρ and coefficient of variation 0·4. The risk population of the areas are chosen to be constant or different, with or without spatial correlation

and (b)). Note that when the risks are spatially independent ($\rho = 0$), Moran's I actually has the nominal type I error probability for any risks variability pattern, since it tests only spatial independence. Testing the situation of risks heterogeneity, I^*_{pop} is naturally more powerful when the risks are more variable. Since these tests are not testing the same hypothesis, it is not correct to compare the power of Moran's I and I^*_{pop} directly.

Note also in Figures 3(a) and (b) that, for high risk correlation degree ($\rho = 0{\cdot}7$), the tests lose power as the coefficient of variation (CV) decreases. This is so because in the limit as CV goes to zero the homogeneity implies spatial independence.

To find a better basis to compare the power of the two tests to detect spatial correlation, we propose a partition of Oden's I^*_{pop} power. Consider the I^*_{pop} power curve varying with the increase of the risks' heterogeneity (Figure 3(b)). We can see this curve broken down in two parts:

(a) The power curve when there is no spatial correlation ($\rho = 0$), which can be considered as detecting only heterogeneity on the rates.

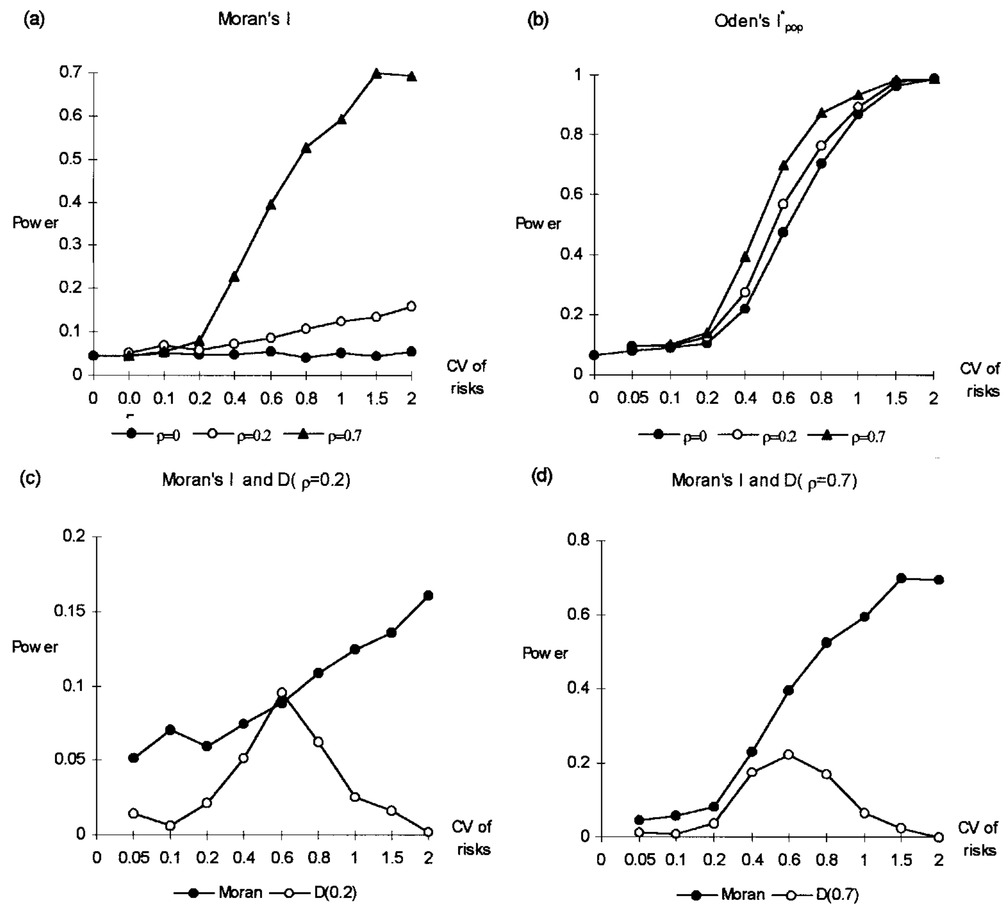

Figure 3. Power estimates of one-sided tests ($\alpha = 0{\cdot}05$) with (*a*) Moran's I and (*b*) Oden's I^*_{pop} based on 1000 simulations. The risks follow the SAR model with mean $4{\cdot}75/10^5$ and varying ρ and coefficient of variation. (*c*) and (*d*) $D(\rho) = \beta(\rho) - \beta(0)$ where $\beta(\rho)$ is Oden's I^*_{pop} power estimated at ρ

(b) The difference $D(\rho)$ between the power curve for a given ρ and the first component above. This difference would detect spatial correlation after controlling for the rates heterogeneity.

The power curve of Moran's I can then be compared with part (b) of I^*_{pop} as defined above (Figures 3(c) and (d)). Using this approach, Moran's I seems to be better suited to detect spatial autocorrelation at the level of spatial units considered. The difference component associated with I^*_{pop} is very small and is close to zero when the risks' variability is large.

3. A NEW PROPOSAL TO ADJUST MORAN'S I

Let $\theta_1, \ldots, \theta_m$ be the unknown and possibly different underlying rate of the areas. Suppose the number n_i of observed events during a reference period has a Poisson distribution with conditional mean $E(n_i \mid \theta_i) = x_i\theta_i$. The estimated rate p_i has conditional mean $E(p_i \mid \theta_i) = \theta_i$ and

Table III. Type I error probability estimate of EBI test (and 95 per cent confidence interval) of one-sided test ($\alpha = 0{\cdot}05$) based on 1000 simulations of constant risk or independently generated risks according to a log-normal distribution with mean θ and coefficient of variation equal to 0·4

Real risks	Constant population	Variable populations without spatial structure	Variable populations with spatial structure
Constant $= \theta$			
$\theta = 4{\cdot}75/10^5$	5·6 (4·2; 7·0)	4·7 (3·3; 6·1)	5·1 (3·7; 6·5)
$\theta = 4{\cdot}75/10^4$	4·7 (3·3; 6·1)	4·8 (3·4; 6·2)	5·1 (4·7; 7·3)
$\theta = 4{\cdot}75/10^3$	5·3 (3·9; 6·7)	5·3 (3·9; 6·7)	5·2 (3·8; 6·6)
Log-normal, mean $= \theta$			
$\theta = 4{\cdot}75/10^5$	4·9 (3·5; 6·3)	5·3 (3·9; 6·7)	5·1 (3·7; 6·5)
$\theta = 4{\cdot}75/10^4$	4·6 (3·2; 6·0)	5·7 (4·3; 7·1)	5·5 (4·1; 6·9)
$\theta = 4{\cdot}75/10^3$	5·3 (3·9; 6·7)	5·2 (3·8; 6·6)	5·7 (4·3; 7·1)

variance $\mathrm{var}(p_i \mid \theta_i) = \theta_i/x_i$. Therefore, the estimated rates have different conditional means and variances.

Adopting a mixing approach, suppose the underlying rates θ_i have *a priori* expectation and variance equal to β and α, respectively. Hence, the marginal expectation of p_i is β and the marginal variance is $\alpha + \beta/x_i$. Now, only the variances differ among the areas and it increases as the population decreases.

Marshall[18] proposed moment estimates for the parameters α and β given by $a = s^2 - b/(x/m)$ and $b = n/x$, respectively, where $s^2 = \sum x_i(p_i - b)^2/x$. Therefore, the marginal expectation and variance of p_i are estimated by b and $v_i = a + b/x_i$, respectively. By convention, if $v_i < 0$, we set $v_i = b/x_i$.

Instead of using the rates p_i, we propose a new index using a deviation of the estimated marginal mean standardized by an estimate of its standard deviation:

$$z_i = \frac{p_i - b}{\sqrt{v_i}}.$$

The *Empirical Bayes Index* (*EBI*) is defined as

$$\mathrm{EBI} = \frac{m}{\sum w_{ij}} \frac{\sum w_{ij} z_i z_j}{\sum (z_i - \bar{z})^2}.$$

Like Moran's I, EBI will tend to be positive if the risks are spatially correlated. The test of spatial independence against the null hypothesis $H_0 : A \cup B$ depends on the null distribution of EBI, which can be obtained by permutation. In this case, we independently permute the vector $(z_1, z_2, \ldots, z_m)$ around the areas a large number of times. For each permuted map, we calculate the value of EBI. The realized p-value is given by the proportion of times EBI exceeds the observed EBI calculated out of the actual map.

3.1. Results of simulations with EBI

Using the same simulation framework defined previously, we analyse the performance of our EBI statistics. Table III shows the results of the type I error probability of our test based on 1000 simulations with constant risk or risks generated as independently and identically random variables

Table IV. Power estimate of one-sided EBI test ($\alpha = 0{\cdot}05$). The estimate is based on 500 simulations of SAR generated risks with expected value θ, coefficient of variation equal to 0·4 and spatial correlation ρ. The risk population of the areas are chosen to be constant or different, with or without spatial correlation

Real risks	Constant population			Variable populations without spatial structure			Variable populations with spatial structure		
ρ	$\theta = 4{\cdot}75/10^5$	$\theta = 4{\cdot}75/10^4$	$\theta = 4{\cdot}75/10^3$	$\theta = 4{\cdot}75/10^5$	$\theta = 4{\cdot}75/10^4$	$\theta = 4{\cdot}75/10^3$	$\theta = 4{\cdot}75/10^5$	$\theta = 4{\cdot}75/10^4$	$\theta = 4{\cdot}75/10^3$
0·1	5·4	10·2	11·4	8·2	9·2	9·0	3·6	8·2	13·0
0·2	7·2	14·0	22·8	6·0	13·4	22·0	4·8	12·4	22·8
0·3	7·4	25·4	43·4	7·2	21·8	40·2	7·4	20·6	40·8
0·4	9·8	32·6	62·8	9·4	22·6	57·8	7·4	26·6	54·8
0·5	8·4	45·8	82·2	8·4	38·4	77·2	8·4	35·4	74·6
0·6	11·0	64·0	94·4	8·8	54·2	86·8	10·0	50·8	87·8
0·7	12·2	75·8	98·0	13·8	58·6	96·2	12·4	63·6	96·4
0·8	16·4	85·2	99·6	17·0	73·4	98·8	14·6	71·4	99·0
0·9	19·8	88·4	99·8	19·0	79·2	98·8	17·8	78·0	99·2
0·95	16·8	79·2	99·6	13·6	72·2	99·2	14·0	73·8	99·4

with log-normal distribution with mean θ and variation coefficient 0·4. The test is one-sided and was carried out under the nominal value of 0·05. Table III shows that, in all risk scenarios, the EBI test kept the type I error probability within the nominal value.

The results for the power against SAR generated risks are shown in Table IV and displayed graphically in Figure 4. We can see that EBI has a substantially larger power than Moran's I when the risk population is heterogeneous. When the population is constant, the two tests have approximately equal power.

4. AN EXAMPLE: HOMICIDES IN BELO HORIZONTE

A broad concept of health considers crime as a component of environmental risk. In Belo Horizonte, there has been concern about the geographical distribution of the several types of crime and we have been involved in spatial analysis of crime rates and covariates. The data set we use in this paper has an interesting outlier which turned out to show an additional property of our test.

The number of homicides in Belo Horizonte in 1994 varies from 0 to 6 cases with an average of 1·3 cases per UP, and hence the homicide rates are small. Thirty-five UPs had a rate equal to 0, while 45 other UPs had rates between 1 and 39 cases per 100,000 inhabitants. One UP was an outlier, with one homicide among 160 inhabitants which produced a rate equal to 625 per 100,000 (Figure 1).

To test for spatial independence of homicide rates through Moran's I, we consider two UPs as neighbours if they are adjacent defining therefore a symmetric W matrix. The value of Moran's I is 0·0129, with p-value 0·039 with 1000 permutations. If the test is carried out with the less acceptable asymptotic normal distribution as the reference distribution, we find a p-value of 0·346. To calculate I^*_{pop}, we defined matrix M equal to W but with the main diagonal set equal to 2. Oden's index is then $5{\cdot}9\times10^{-6}$ with p-value 0·0102. Hence, both indexes lead us to conclude that Belo Horizonte homicide rates in 1994 show evidence of spatial correlation. Waldhör's test has p-value equal to 0·244. The value of EBI is 7·866 with permutation p-value equal to 0·167, non-significant at the usual levels.

The discrepancy of conclusions can be explained by the presence of the high outlier in a sparsely populated area and singled out in the map. Excluding this area from the data, we find Moran's I equal to $-0{\cdot}070$ with p-value 0·824 under permutation, and, using the normal distribution as reference, we find a p-value equal to 0·810. Oden's index is equal to $2{\cdot}20\times10^{-6}$ with p-value 0·165, and Waldhör's test gives a p-value of 0·90. The EBI statistic is equal to $-5{\cdot}618$ with p-value equal to 0·786. The significant results of Moran's and Oden's test disappears but our EBI test is not affected by the outlier removal. Hence, we find out that our proposed statistic has some additional robustness qualities due to its shrinkage effect on the crude rates.

5. CONCLUSIONS

In this work, we consider tests for the hypothesis of spatial independence of morbidity risks. The permutation test based on Moran's I applied directly on the observed rates loses power if the areas have risk populations of different sizes. However, the power is not additionally affected if, in addition to being different, the populations are also spatially correlated.

We verify the effect of varying populations in the type I error probability of the permutation test when the underlying risks are equal for all areas. In our simulations, the actual type I error probability is smaller than its nominal value when the populations are different without spatial

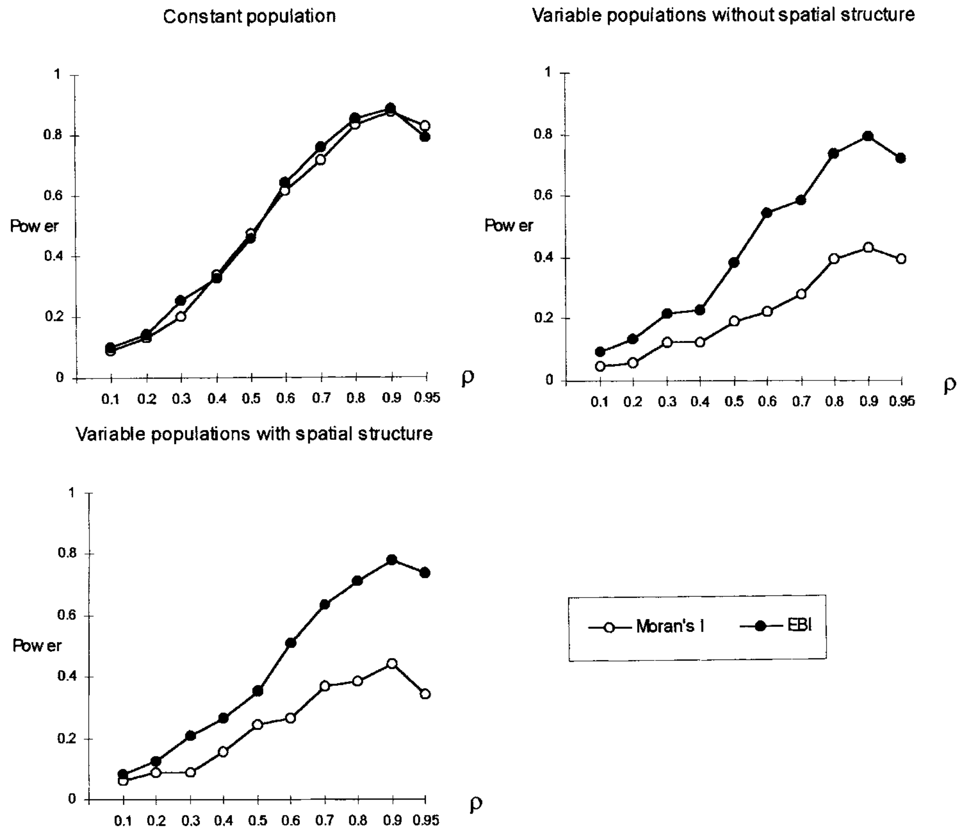

Figure 4. Power estimates of one-sided tests with EBI statistic with $\alpha = 0{\cdot}05$ based on 500 simulations with mean risk equal to $4{\cdot}75/10^4$

structure. When the populations are spatially correlated, Moran's I has type I error probability greater than the nominal value.

We introduce a proposal to adjust Moran's I for the variation on population size. The adjustment is based on a Bayesian approach to model the underlying risks allowing for realizations with different risks between the areas. The permutation test based on the new index has a larger power than Moran's I applied directly on the observed rates. Additionally, the type I error probability of our test is within the nominal significance level in all simulated situations.

We show that two previous proposals to adjust Moran's I, Oden's I^*_{pop} and Waldhör's I statistic, have some problems. Oden's test is very powerful to test risk heterogeneity but its power does not increase substantially when, in addition to their heterogeneity, the risks are also spatially correlated. The spatial correlation interpretation of a significant Moran's I test implies that close areas tend to have similar risks, producing a thematic map with clusters of similar values. If this test accepts H_0 we can have homogeneous or heterogeneous risks. In the case of I^*_{pop}, the null hypothesis rejection means heterogeneous risks, which can be either spatially correlated or not. Oden[13] states that if the risks are heterogeneous and spatially independent, we have a case of disease clustering, that is, concentration of a few cases in a few areas, even if they are far apart. However, if we want to test only spatial independence at the areas' own scale, we should use Moran's I or our proposed test to be sure of interpreting the null hypothesis rejection as evidence of spatial correlation of risks, which also implies its heterogeneity.

The other proposal, Waldhör's I, has an error type I probability larger than its nominal value and in general cannot be trusted.

Finally, note that the power against spatial correlation of very low risks of Moran's I or any other test is low, due to the resulting great number of rates equal to zero. Additionally, since risks homogeneity implies spatial independence, the tests are likely to be more powerful to detect spatial correlation when the risks have large variability.

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