Adding Structural Variables to Space-Time Interaction Tests: An Application to Fertility Transition in Brazil

Carl Schmertmann, Florida State University
Renato Assunção, Universidade Federal de Minas Gerais
Joseph Potter, University of Texas

OBJECTIVE

Does fertility decline in a population as a predictable response to economic and social changes, or from a contagious process of social interaction that spreads new ideas and behavior through interpersonal contacts? This has been a central and sometimes contentious question in demography. The two processes are not mutually exclusive, of course, and there is now a fairly strong consensus that both structural change and ideational diffusion play a role in fertility transition (Casterline 2001:3).

Maps sparked much of the initial structural-diffusion debate. Main findings from Princeton's European Fertility Project (Coale and Watkins 1986) included (1) that provincial-level fertility change was not well predicted by provincial-level economic trends, and (2) that fertility decline began at widely different levels of development across the continent, often starting in clusters of contiguous provinces and spreading across the map over time.

Recent demographic research has returned to maps, focusing specifically on the onset of fertility decline as an epidemic process (Guilmoto and Rajan 2001; Boquet-Appel and Jakobi 1998; Balabdoaui et al. 2001; and Boquet-Appel et al. 2002). In this paper we argue that a standard statistical test used in some of these recent studies (Knox 1964) is inappropriate for assessing the presence of spatial diffusion in fertility decline. We propose a modification to the Knox test that accounts for spatial and temporal changes in underlying structural variables.

We illustrate with an application to fertility transition and economic change in twentieth-century Brazil. However, the statistical procedure that we develop is quite general. It is applicable for studying any process – demographic, biological, or social – in which spatial diffusion could be affected not only by person-to-person contact, but also by changes in local levels of important covariates.

THE KNOX TEST

Definition

Events generated by epidemics (social or biological) exhibit characteristic patterns of change over sequences of maps. If physical proximity is necessary for transmitting an infectious agent (idea or virus), then new cases occurring at similar times will also tend to occur in nearby places. Consequently, a contagious process generates a changing spatial

distribution of incidence over time. In contrast, if a process is not contagious and proximity is irrelevant to occurrence (for example, new cases of a genetic disease), then the spatial pattern of events could remain constant over a long sequence of maps. The presence of *space-time interaction* in event data is therefore a key indicator of an infectious pattern.

Knox (1964) proposed a simple and still widely used statistical test for space-time interaction in health-related events. For the Knox test we consider a map with n locations indexed by i=1…n. Each location has a single event time t_i ; in our applications t_i indicates the onset of fertility decline. We define a function d_{ij} measuring distance between locations (or equivalently, between events) i and j, and we define dummy indicators

$$\delta_{ij} = \begin{cases} 1 \text{ if } d_{ij} \le D \\ 0 \text{ otherwise} \end{cases} \qquad \text{and} \qquad \tau_{ij} = \begin{cases} 1 \text{ if } \left|t_i - t_j\right| \le T \\ 0 \text{ otherwise} \end{cases}$$

to represent pairs of events that are *close in space* and *close in time*, respectively. Note that these definitions of closeness depend on the chosen cutoff values D and T.

The idea of the Knox test is that an infectious process should exhibit space-time interaction, indicated by a relatively large number of event pairs (i,j) for which both δ_{ij}=1 and τ_{ij}=1. The Knox statistic X is simply the count of unique event pairs that are close in both space and time:

Event Pairs (*I*, *j*)	Close in Space	
Close in Time	No (δ_{ij}=0)	Yes (δ_{ij}=1)
No (τ_{ij}=0)	--	--
Yes (τ_{ij}=1)	--	$\mathbf{X} = \sum_i \sum_{j>i} \delta_{ij}\, \tau_{ij}$

A single event can contribute many times to this sum as it is paired with other events, resulting in non-independent observations that depend on map relationships in complex ways. It is therefore difficult to derive an analytical distribution for X under the null hypothesis of no space-time interaction.

The standard Knox procedure circumvents this difficulty by using Monte Carlo simulation to approximate the null distribution of X. To produce a Monte Carlo sample the computer generates a random reordering of event times $t_{(1)}…t_{(n)}$ (such as t_6, t_{138}, …, t_{15}), assigns the rearranged times in order to locations $1…n$, and then calculates the Knox statistic for the corresponding map. Each permutation would be equally likely under the assumption that event times are unrelated to their locations. The computer recalculates a Knox statistic X_b for each of b=1…B permutations, and the estimated p-value is the proportion of datasets (including the observed one) for which $X_b \ge X_{obs}$. A small p-value is evidence of space-time interaction.

Demographic Applications

In demography, the most important applications of the Knox test have been in studying fertility transitions. Bocquet-Appel and Jakobi (1998) analyzed the geographical pattern of fertility change in 78 counties of Great Britain between 1861 and 1901. They generated a sequence of smoothed maps of the I_g fertility index for the five census years between 1861 and 1901, and from those maps estimated the time at which each county began its fertility transition. They used Knox statistics to test for spatial diffusion of fertility control, and found strong evidence of space-time interaction in onset times (p=.002 or .001, depending on distance cutoff D). Thus, nearby counties tended to have similar onset times, as in a typical contagion process. Bocquet-Appel and Jakobi (1998) concluded that fertility decline in Britain was a geographical diffusion process with characteristics of a social epidemic.

Applying a similar statistical test to India, with data for several hundred districts from 1961 to 1991, Bocquet-Appel and colleagues concluded that the fertility transition there did not show a pattern of geographical diffusion (Balabdoaoui, Bocquet-Appel, Lajaunie, and Rajan 2001; Bocquet-Appel, Rajan, Bacro, and Lajaunie 2002). Because space-time interaction is weak in the Indian maps, these researchers attribute fertility decline in India mainly to non-contagious processes, such as nationwide family planning policies.

Problems in the Presence of Spatially-Patterned Structural Change

The Knox test has advantages that make it popular among epidemiologists and biostatisticians. It does not require population risk data. It is unaffected by purely temporal variations in diagnosis or reporting, or by purely spatial variations in population distribution. Like any well-established method, however, the Knox test has been critiqued and extended. Several papers have offered proposals to relax dependence on arbitrary spatial and temporal thresholds D and T (Mantel 1967, Baker 1996, Kulldorff and Hjalmars 1999, Diggle *et al.* 1995, Jacquez 1996). Others have considered how to appropriately modify the Knox test when the spatial distribution of the risk population varies over time (Mantel 1967, Roberson and Fisher 1983, Klauber and Mustachi 1970, Kulldorff and Hjalmars 1999).

To date, however, researchers have not addressed potential confounding from spatially varying covariates that influence events. Changing local conditions may have negligible effects in epidemiological applications involving very short time periods, but they can be very important in demographic applications studying transitions over decades. Local economic and social conditions that affect fertility rates might typically exhibit strong spatial heterogeneity, and this would confound the analysis and compromise any finding of space-time interaction. As a simple example, an apparent 'outbreak' of low fertility in a cluster of regions could be caused by a parallel 'outbreak' of female education in those same areas. Because the central question in demographic applications of the Knox test is the importance of diffusion relative to effects of structural changes, failure to account of the space-time interaction induced by covariates is a potentially serious flaw.

A MODIFIED KNOX TEST INCLUDING COVARIATES

Locations may have observable characteristics that are predictably related to event times. In this case, differences in local characteristics alone could cause space-time clustering, and the standard Knox procedure (which looks for any space-time interaction from any source) is an inappropriate test for epidemic patterns.

We propose a generalization of the Knox test that models relationships between outcomes and covariates. Given that model, we test for *unexpected* space-time clustering, net of covariate effects.

Specifically, we model local-level demographic transition as a proportional hazard process (Cox 1972), in which an irreversible transition to a low-fertility regime begins in location i during any period t with hazard rate

$$\lambda_{it} = \lambda_t^* \exp(\beta' x_{it})$$

where λ_t* is a non-parametric baseline hazard common to all locations during period t, and x_{it} is a vector of relevant characteristics for location i in period t.

Under this model, expected transition times are random over the map only when $\boldsymbol{\beta}=\mathbf{0}$. Otherwise, we would expect space-time interactions in transitions (to the extent that they are caused by space-time patterns in covariates) even in the absence of epidemic diffusion.

Rather than describe the process in detail, in this extended abstract we give only the essential outline of our modified Knox test:

(1) Estimate β from observed data using a Cox proportional hazards model

(2) Modify the Monte Carlo simulations described in section 2 above, by drawing orderings $t_{(1)}\ldots t_{(n)}$ *with the probabilities implied by the estimated* β.

(3) Record the proportion of re-ordered samples in which the simulated Knox statistic X_b exceeds X_{obs}.

Step (2) is the key. In the standard Knox test $\boldsymbol{\beta}=\mathbf{0}$, structural variables are unrelated to transition times, and – under the null hypothesis of "no epidemic spread" – all orderings of observed times would be equally likely. In our more general version $\boldsymbol{\beta}\neq\mathbf{0}$, and differences in structural variables over space and time make some orderings much more likely than others under the null hypothesis. For example, if we find that high levels of household electrification increase the hazard of fertility transition, then our Monte Carlo samples will be much more likely to assign the early transition times from the observed $\{t_1\ldots t_n\}$ to regions with high electrification. If these electrified regions are clustered on the map, then simulated Knox values X_b will be high in many reorderings, thus "explaining away" one source of space-time clustering. Only *additional* clustering, not predictable from covariates, provides evidence for diffusion.

PRELIMINARY RESULTS FROM BRAZILIAN DATA

To illustrate our method, we use Brazilian Demographic Census microdata from 1960, 1970, 1980, and 1991 to calculate fertility rates along with the average levels of a number of key indicators of development for 518 microregions at each census date. The data are drawn from a long-form questionnaire that collected information on births to women of reproductive age. A full description of estimation procedures can be found in Potter, Schmertmann, and Cavenaghi (2002).

We defined a pair of regions as "close in space" if they were adjacent on the map, or if the distance between centroids was less than 200 km. With 518 regions there are 518*517/2 = 133903 distinct pairs, of which 4651 are "close in space" under this definition.

To define the onset of fertility decline, we used the following algorithm: In 1960, the first census in our series, a microregion was classified as already having entered fertility decline if its estimated TFR was below 4.5. In succeeding years, onset was defined in terms of the TFR either being below 4.5, or having fallen by more than a 20% between the two censuses. Under this definition there were 34 transitions before 1960, 61 transitions over 1960-1970, 193 over 1970-1980, 193 over 1980-1991, and 37 microregions had not yet entered transition by 1991.

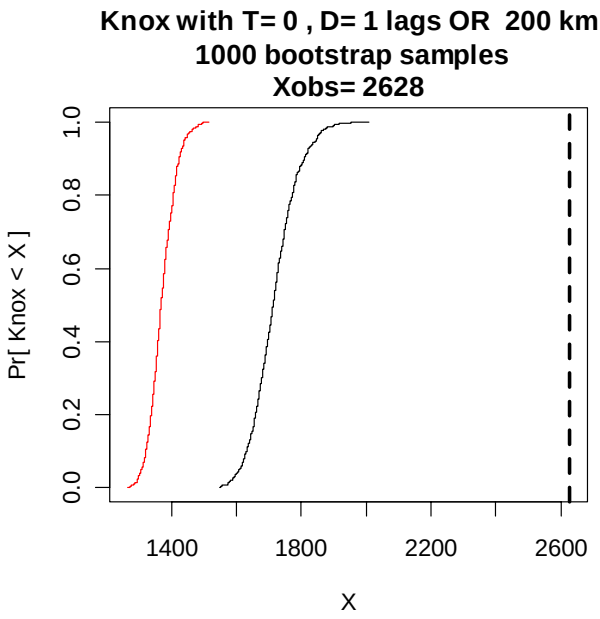
Defining a pair of transitions as "close in time" if they happened in the same intercensal period, the observed Knox statistic for our map sequence is X_{obs}=2628. Applying the standard permutation test, we find extremely significant space-time clustering: of 1000 Monte Carlo reorderings, none produced Knox statistics above 2628 (the mean simulated value was 1371, and the maximum was 1514).

Using four independent covariates (described in Potter et al. 2002) as proxies for structural change, and estimating a proportional hazards model for fertility transition yields:

	Coefficient	*Exp(Coefficient)*	*SE*	*p*
Household Electrification	2.92	18.55	0.388	5.7e-14
Female LF Partic	-1.83	0.16	0.9347	5.0e-02
Female Education	0.39	1.47	0.0785	8.0e-07
Proportion Catholic	-2.57	0.08	0.7775	9.4e-04

We then perform the Knox test again, this time modifying the probabilities of selecting different orderings $t_{(1)}\ldots t_{(n)}$ according to these estimated β values. For example, when we select the 34 areas that will be assigned "1960" transitions in a simulation, it is most likely that these will be areas that had high 1960 levels of electrification, low (?? we are still pondering the sign of this coefficient at PAA submission time…) 1960 levels of female LF participation, high levels of female education, and low levels of Catholicism.

We find that correcting the Knox test to include these covariates does not eliminate the strong evidence for an epidemic pattern of fertility decline across the map. The figure below compares the simulated distribution of the Knox under the usual null (times unrelated to locations; red, left-hand curve), the distribution under the modified null (times related to locations through structural variables only; black, right-hand curve), and the observed Knox value in the Brazilian map sequence (dashed vertical line). Even after including covariates, none of 1000 Monte Carlo simulations of the Knox statistic produced a map with $X_b > X_{obs}$=2628. Simulated Knox statistics were considerably higher with covariates included (the mean simulation was 1716 and the maximum was 2009, compared to 1371 and 1514 for the standard Knox simulation).



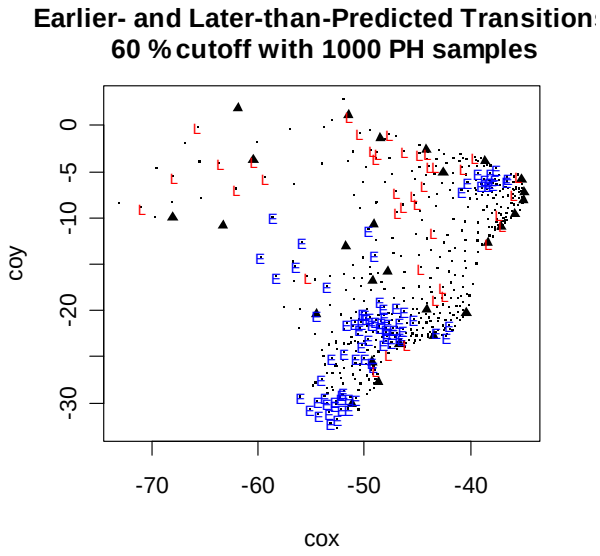
In a sense, this figure allows us to see what portion of the 'epidemic' pattern in fertility transition is explained by space-time patterns in the model's four covariates. In this case, covariates clearly matter, but there is still extremely strong, unexplained space-time correlation. In short, this spatial analysis suggests that there is still room for a "diffusion" explanation of fertility change, even after controlling for important structural factors.

The Knox+covariate simulation also opens another analytical possibility that we will explore in the paper. Specifically, we know covariate values for the 518 Brazilian microregions in all four censuses, and we have an observed transition time (possibly censored at 1991) for each location. By comparing each region's *observed* time to its many *simulated* times in the Knox+ permutation samples, we implicity compare when it *did* have its transition to when it likely *would* have had its transition as predicted by local covariates. Such comparisons, when mapped, may provide information about where and when the spatial clustering detected by the Knox+ test occurred.

For exploratory purposes, we used the 1000 Knox+ Monte Carlo samples depicted in the black line in the previous figure. We denote observed transitions as *early* if more than 60% of the simulated transitions in that area were in a later decade, and *late* if more than 60%

of simulated transitions happened in earlier. This procedure identifies 82 transitions that were unexpectedly early considering local covariate levels, and 40 that were unexpectedly late.

The small map shows the location of the early (E) and late (L) transitions, the locations of other microregions (dots), and the locations of state capitals (triangles). The clusters of E regions in the South and Southeast correspond to the hinterlands around Sao Paulo and Porto Alegre, two large cities that were important initial foci of low fertility. The spatial arrangement of these southern *E*s is very suggestive of a diffusion process – these were less-developed regions near initial areas of low fertility, and their fertility transitions occurred earlier than one would predict from local development indicators. The patch of *E*s in the Northeast is extremely interesting: it represents 1970 transitions in a cluster of very poor regions, and is probably related to local reproductive health policies.



We emphasize that building a method that identifies this Northeastern cluster of early transitions is already an advance. We will investigate the reasons for the cluster in more detail before PAA.

DISCUSSION AND CONCLUSION

Transitions in demographic behavior have been a central focus of population studies for many decades. There have been many attempts to explain how and why fertility and mortality have evolved through space and time in virtually all regions of the world. Yet major debates persist. Increasing availability of geographically referenced data for relatively long time series, together with development of appropriate statistical methods for analyzing spatial time series data, can help to address some of the fundamental questions in these debates.

In the past, most demographic analysis has either relied on maps, or statistical methods that do not account for spatial as well as temporal proximity. While spatial statistics and spatial econometrics are now well developed fields that clearly have potential to further understanding of demographic transitions, many of the methods and procedures have been developed for use in other contexts. Before bringing them to bear on the analysis of demographic transitions, they may require some adaptation. We believe the Knox statistic is just such a case: it was developed for use mainly in epidemiological applications with a relatively short time horizon, and in which contagion was a relatively likely and rapid

phenomenon. Bocquet-Appel and colleagues (Bocquet-Appel and Jakobi 1998; Bocquet-Appel, Rajan, Bacro, and Lajaunie 2002) were astute in recognizing that the technique might be usefully applied in the analysis of fertility transitions. However, they seem to have overlooked what appears to us to be an important vulnerability of the method in this new setting.

In this paper, we develop a modification of the Knox test that adjusts for spatial patterns and trends in measurable covariates of fertility, and apply the modified method to real data. The proposed modification apparently leads to a substantial difference in the location of the null (='no diffusion') reference distribution, but does not change the conclusion reached by the standard test. It is possible that our hazard model omits relevant covariates that also have some spatial structure. Thus, there are grounds for caution in interpreting even this modified Knox test, and further work to assess the sensitivity of the new measure to unmeasured spatial heterogeneity of causal factors may be warranted. At the least, we have taken an important first step toward resolving the major weakness of the Knox test for demographic applications.

But we also hope that we will illuminate the role that tests for space-time interactions and related spatial statistics methods can play in population studies. By actually identifying space-time clusters, we can use this methodology to point to the times and places in which diffusion appears to have been important. Moreover, as we have shown (or will show in the full version of the paper), doing so raises interesting substantive questions about what was actually going in those places and times.

REFERENCES.

Baker RD (1996) Testing for space-time clusters of unknown size. *Journal of Applied Statistics*, 23, 543-554.

Balabdaoui, F., Bocquet-Appel JP, Lajaunie C and Rajan SI (2001) Space-time evolution of fertility transition in India (1961-91). *International Journal of Population Geography*, 7, 2 : 129-148.

Bhopal RS, Diggle PJ, Rowlingson BS (1992) Pinpointing clusters of apparently sporadic Legionnaire's disease. *British Medical Journal*, 304, 1022-1027.

Birch JM, Alexander FE, Blair V, Eden OB, Taylor GM, McNally RJQ (2000) Space-time clustering patterns in childhood leukaemia support a role for infection. *British Journal of Cancer*, 82, 1571-1578.

Bocquet-Appel JP, Jakobi L (1998). Evidence for a spatial diffusion of contraception at the onset of the fertility transition in Victorian Britain. *Population: An English selection, Special issue New advances in Social Sciences*, 10(1), 181-204.

Bocquet-Appel JP, Rajan IS, Bacro JN, Lajaune C (2002) The onset of India's fertility transition. *European Journal of Population*, 18, 211-232.

Casterline, JB (2001). Diffusion processes and fertility transition: Introduction, in JB Casterline (ed.), *Diffusion Processes and Fertility Transition: Selected Perspectives*. National Academy Press. Washington DC.

Coale, AJ and Watkins, SC, eds. (1986). *The decline of fertility in Europe*. Princeton, NJ: Princeton University Press.

Cox, DR (1972). "Regression Models and Life Tables (with Discussion)". *Journal of the Royal Statistical Society, Series B* 34:187-220.

Diggle PJ, Chetwynd AG, Häggkvist R, Morris SE (1995). Second-order analysis of space-time clustering. *Statistical Methods in Medical Research*, 4, 124-136.

Guilmoto, CZ and Rajan SI (2001) Spatial patterns of fertility transition in Indian districts. *Population and Development Review*, 27, 4 : 713-738.

Jacquez, GM (1996) A K Nearest neighbour test for space-time interaction. *Statistics in Medicine*, 15, 1935-49.

Klauber MR, Mustachi P (1970) Space-time clustering of childhood leukemia in San Francisco. *Cancer Research*, 30, 1969-1973.

Knox EG (1964) The detection of space-time interactions. *Applied Statistics*, 13, 25-29.

Kulldorff M, Hjalmars U (1999) The Knox method and other tests for space-time interaction. *Biometrics*, 55 (2): 544-552.

Mantel N (1967) The detection of disease clustering and the generalized regression approach. *Cancer Research*, 27, 209-220.

Montgomery, MR and Casterline JB (1993) The diffusion of fertility control in Taiwan: evidence from pooled cross-sectioned time-series models. *Population Studies*, 47, 457-79.

Morris JK, Alberman E, Mutton D (1998) Is there evidence of clustering in Down syndrome ? *International Journal of Epidemiology*, 27, 495-498.

Norstrom M, Pfeiffer DU, Jarp J (2000) A space-time cluster investigation of an outbreak of acute respiratory disease in Norwegian cattle herds. *Preventive Veterinary Medicine*, 47(1-2): 107-119.

Potter JE, Schmertmann CP, and Cavenaghi SM (2002) Fertility and development: Evidence from Brazil. *Demography,* 39, 739-761.

Roberson PK, Fisher L (1983) Lack of robustness in time-space disease clustering. *Communications in Statistics - Simulation and Computatio*n, 12, 11-22.

Samuelsson U, Johansson C, Carstensen J, Ludvigsson J (1994) Space-time clustering in insulin-dependent diabetes mellitus (IDDM) in South-East Sweden. *International Journal of Epidemiology*, 23, 138-142.

Tolnay, SE (1995) The spatial diffusion of fertility: a cross-sectional analysis of counties in the American South, 1940. *American Sociological Review*, 60, 299-308.

Weeks, JR, Getis A, Hill AG, Gadalla MS, Rashed T (2004) The fertility transition in Egypt: Intraurban patterns in Cairo. *Annals of the Association of American Geographers*, 94, 1 : 74-93.