Differential and enhanced response to climate forcing in diarrheal disease due to rotavirus across a megacity of the developing world

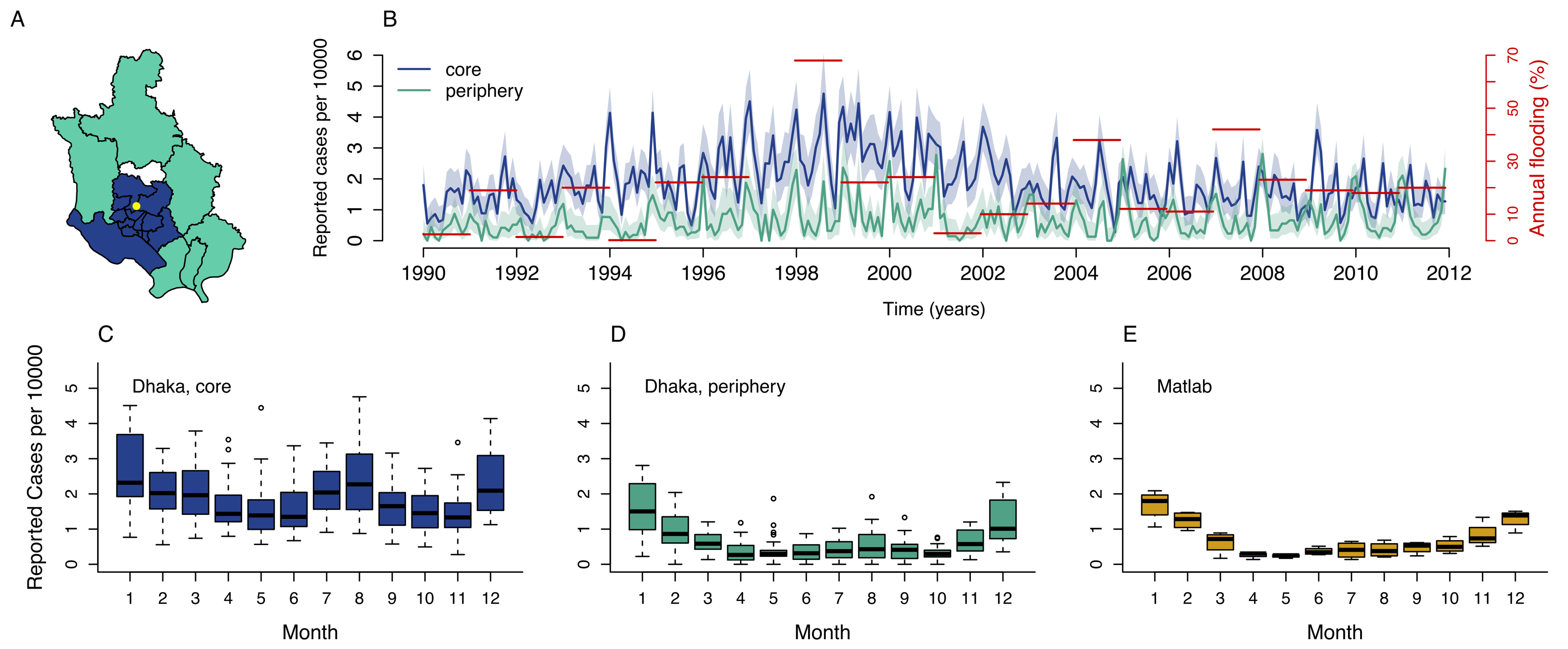
Pamela P. Martinez[1], Aaron A. King[2], Mohammad Yunus[3], A.S.G. Faruque[3] and Mercedes Pascual[1,4]

1 Ecology & Evolution, University of Chicago, Chicago, IL. **2** Ecology and Evolutionary Biology, University of Michigan, Ann Arbor, MI.
3 International Centre for Diarrheal Disease Research, Dhaka 1000, Bangladesh. **4** Santa Fe Institute, Santa Fe, NM.

BACKGROUND

The impact of climate factors on the population dynamics of infectious diseases has typically been addressed at large spatial scales by aggregating surveillance data over whole countries, regions, and cities[1-5]. Global climate drivers, such as the El Niño Southern Oscillation (ENSO), are expected to operate over large spatial scales, synchronizing fluctuations of disease incidence across space (i.e., the Moran effect in population dynamics[6-7]). A recent study has shown however that the spatio-temporal dynamics of cholera in Dhaka, Bangladesh, are not homogeneous at intraurban scales[8].

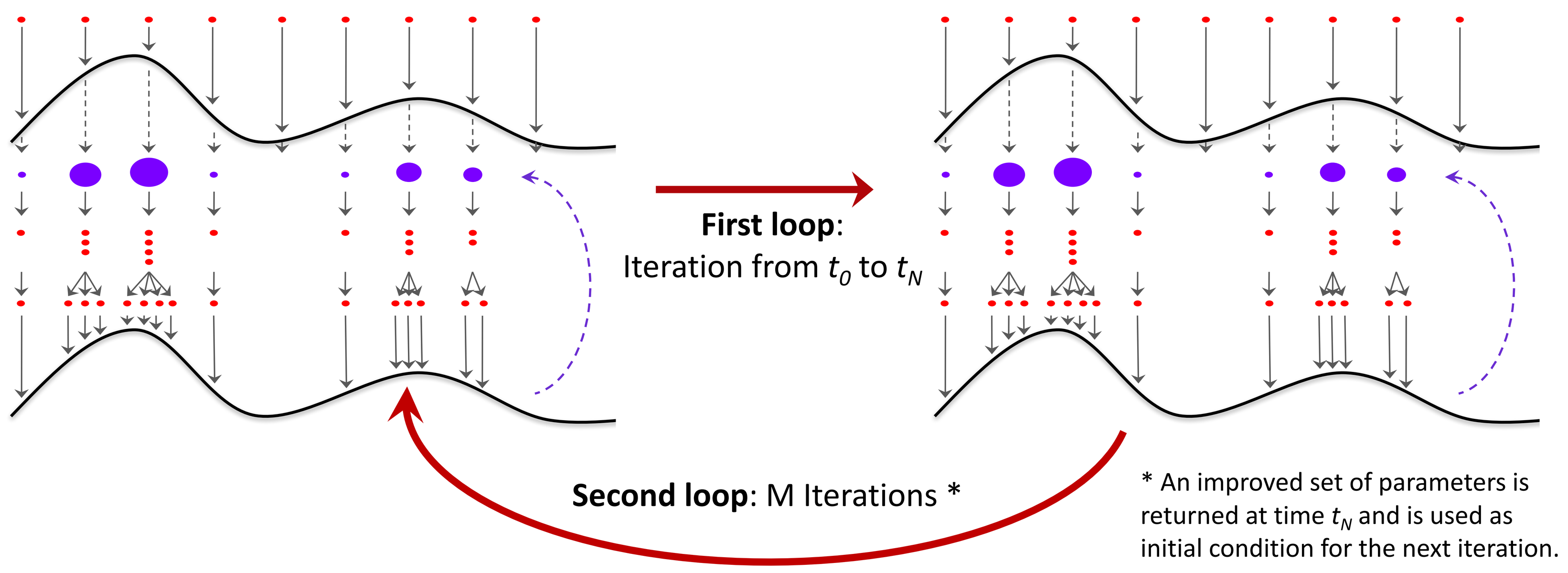
Here, **we examine the role of the monsoons, and in particular flooding, in modulating the transmission of rotavirus.** We inquire into whether such an effect might vary across local scales within a large urban environment.



The aggregation of the 22 years of data by **core** and **periphery** reveals that the incidence rate in the core is almost 3 times that in the periphery. Rotavirus cases in the core exhibit a temporal pattern similar to that described previously for tropical countries, with one peak during winter and another during the monsoon. However, the second peak in cases is less pronounced in the periphery, and less than half the size of the winter peak (57% smaller). A similar seasonal pattern is found in Matlab, a rural area 55km south-east of Dhaka.

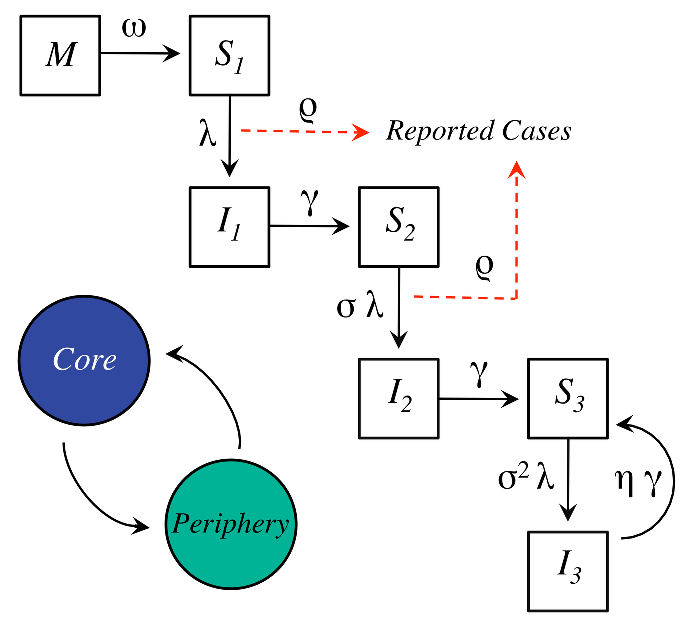
PARAMETER ESTIMATION

The estimation of both parameters and initial conditions for all state variables was carried out with an iterated filtering algorithm (MIF, for maximum likelihood iterated filtering) implemented in the R package "pomp" [partially observed Markov processes]. This algorithm maximizes the likelihood and allows for the inclusion of both measurement and process noise. The initial search of parameter space was performed with a grid of 10,000 random parameter combinations, and the output of this search was used as the initial conditions of a more local search. We repeated this process until the maximum likelihood value was stationary.



TRANSMISSION MODEL

Each population, for core and periphery respectively, is divided into the following classes: Newborn M, Susceptible (S_1, S_2, S_3) and Infected (I_1, I_2, I_3). The effect of movement between populations is incorporated within the force of infection.



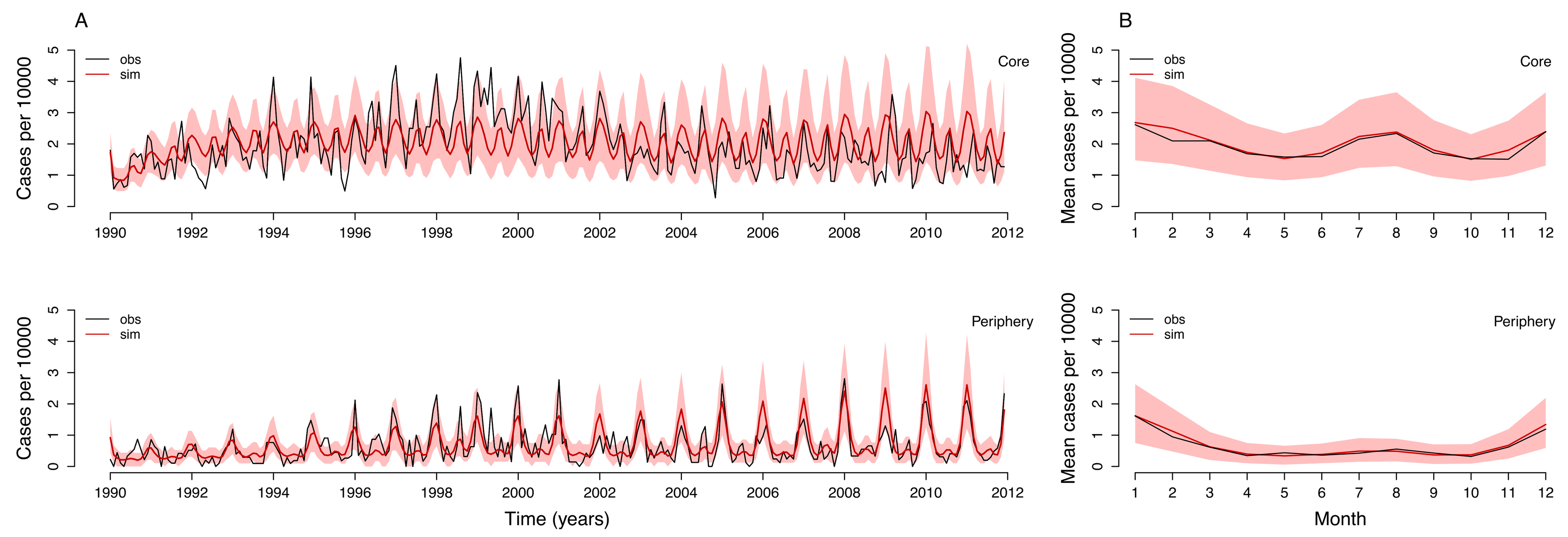
RESULTS

A likelihood-based comparison of the models

The best model includes flooding as a covariate in the transmission rate, which allows for an interannual effect of climate forcing. This model also considers differential seasonality in the core and periphery.

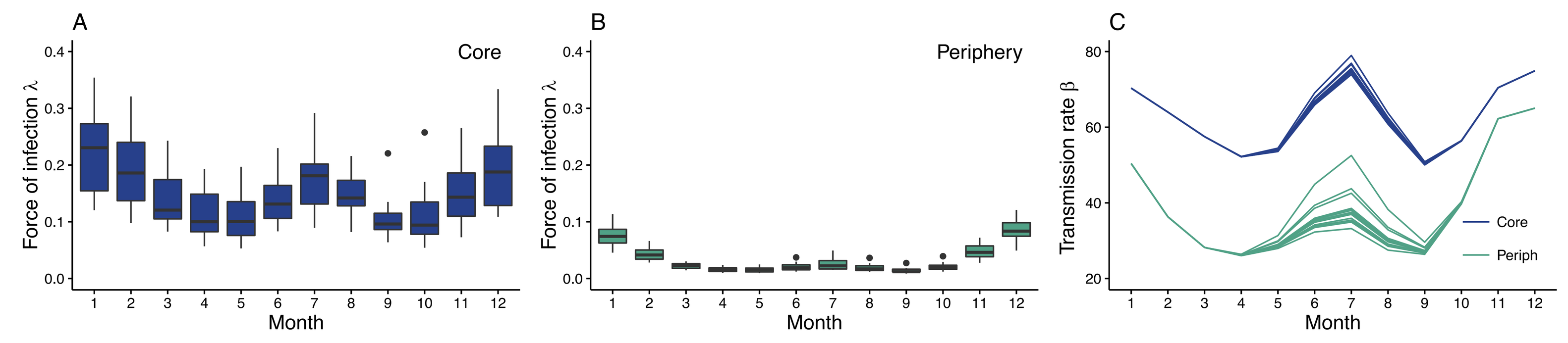
Model	log-likelihood	SE	no. param	AIC	LR Test
With flooding effect	-1577.6	0.33	25	3205.2	
Without flooding effect	-1582.2	0.35	23	3210.4	p-value = 0.01

The best-fitting model captures the interannual variation and the main seasonal pattern of the reported cases in both regions.



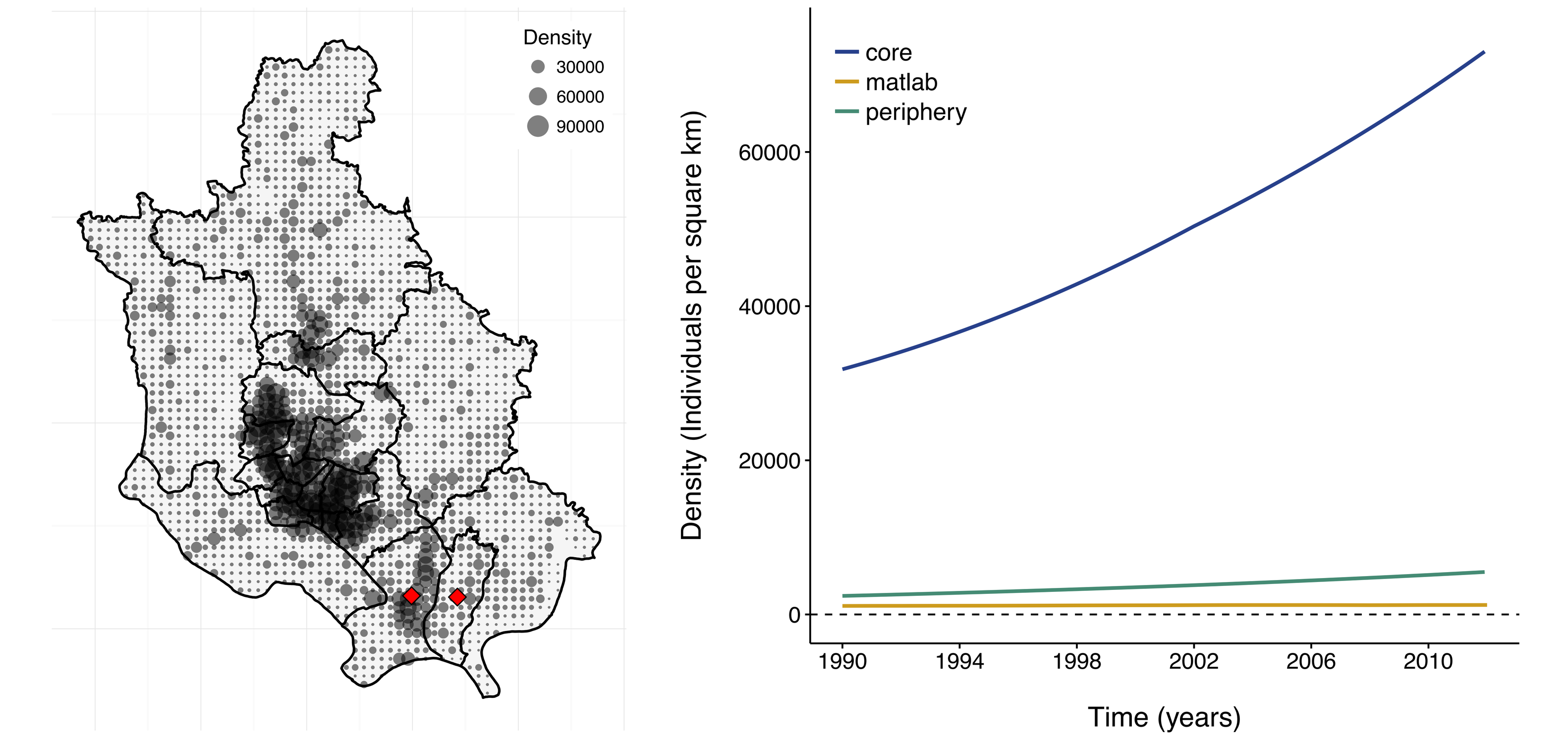
Comparison of the simulated cases for the 'best' model with those reported for the core and periphery of Dhaka. The model simulations are not next step predictions but numerical simulations of the model forward for the whole time period of the study starting with estimated initial conditions.

The core exhibits a higher force of infection and a more 'endemic' pattern in which transmission is sustained during the low season. In addition, the force of infection exhibits a monsoon peak that is largely absent in the periphery. Note however the higher interannual variability of the transmission rate in the periphery.



Force of infection and transmission rate estimated with the best-fitted model.

The core and periphery differ significantly in population density, and the periphery shows values close to those of the rural area South of Dhaka known as Matlab. The temporal patterns of rotavirus dynamics are also similar between Matlab and the periphery of Dhaka. (More intermediate patterns are seen for two peripheral thanas, indicated by the diamonds in the map, whose population density is high in parts of their area).



Population density. (Left) Map of the population density for 2010. Each grey dot refers to the density at a 1 km² resolution. Diamonds in red label the peripheral thanas of Narayanganj Sadar and Bandar. **(Right)** Average population density across thanas within each region.

CONCLUSIONS (Martinez *et al.* (2016) PNAS 113(15): 4092-4097)

- There is pronounced spatial heterogeneity in both the overall magnitude and the seasonal pattern of disease risk within the city. In particular, the core of the city exhibits two peaks per year including a monsoon peak absent in the periphery.
- The two regions of the city, core and periphery, respond differentially to climate forcing, consistent with previous findings for cholera in the same region. The more endemic core of the city experiences a stronger effect of the monsoons seasonally, whereas the more epidemic periphery exhibits an interannual effect, only evident in years with the most extreme climate anomalies (for example, during the 1998 El Niño).
- The distinction of core and periphery based on the dynamics of the disease is congruent with spatial variation in socioeconomic conditions, including population density. It is also consistent with rural vs. urban characteristics as indicated by the comparison to the rural Matlab.
- Besides socio-economic and demographic factors affecting contact patterns and therefore exposure, the two regions of the city might also more directly differ in susceptibility to flooding itself.
- This work also suggests the presence of a transmission reservoir in the core that maintains transmission between seasons and primes the seasonal response of the system to the monsoons.

ACKNOWLEDGMENTS

This work was completed in part with resources provided by the University of Chicago Research Computing Center. This research was partially supported by the National Oceanic and Atmospheric Administration (Grant F020704). The case data used in this paper were collected with the support of the ICDDR,B and its donors, who provide unrestricted support to the ICDDR,B for its operation and research.

REFERENCES

1. Pascual M., X. Rodo, P. Ellner, R. Colwell, M.J. Bouma (2000). Science 289: 1766-1769.
2. Zhou G, Minakawa N, Githeko AK, Yan GY. (2004).Proc Natl Acad Sci USA 101: 237580.
3. Cazelles B, M. Chavez, A.J. McMichael, S. Hales (2005). PLoS Med 2:e106.
4. Koelle K., X. Rodo, M. Pascual, M. Yunus, G. Mostafa (2005). Nature 436: 696-700.
5. Nagao Y. and K. Koelle (2008). Proc Natl Acad Sci USA 105: 2238-2243.
6. Laneri K., A. Bahdra, E. Ionides, et al. (2010) PLoS Comp Biol 6(9): e1000898.
7. Hoshen M. and A. Morse (2004) Malaria Journal. 3: 32-46.
8. Sultan B., K. Labadi, J.F. Guegan, S. Janicot (2005) PLoS Med 2: e6.