Predicting propagation of dengue with human mobility:

A Pakistan case study

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Planning meeting:

"Forecasting propagation of dengue/zika in Sri Lanka with Mobile Network Big Data"

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IDRC CRDI

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UKaid from the British people

The role of human mobility in spreading dengue

- The dengue mosquito has a lifespan of 2-4 weeks and a range less 1km
- Dengue is spread beyond the natural range of the mosquito by the movement of infected hosts
- As a result knowledge of human mobility patterns can shed light on the pattern of dengue propagation and the level of disease incidence in a region

Outline

- Background
- Introduction to case study
- Data
- Methodology

  -Ento-epidemiological model

  -Prediction of dengue importation using travel patterns

  -Epidemic risk maps
- Limitations

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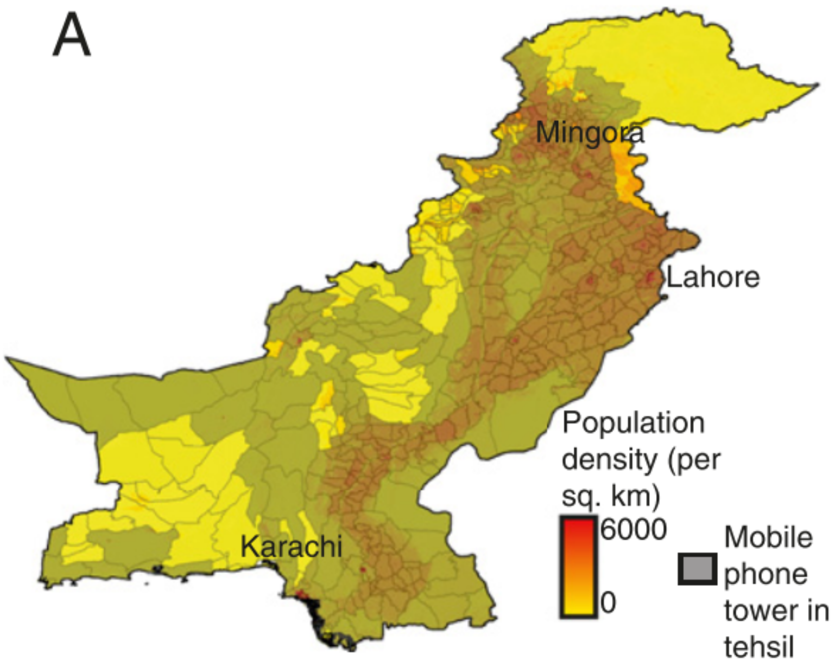
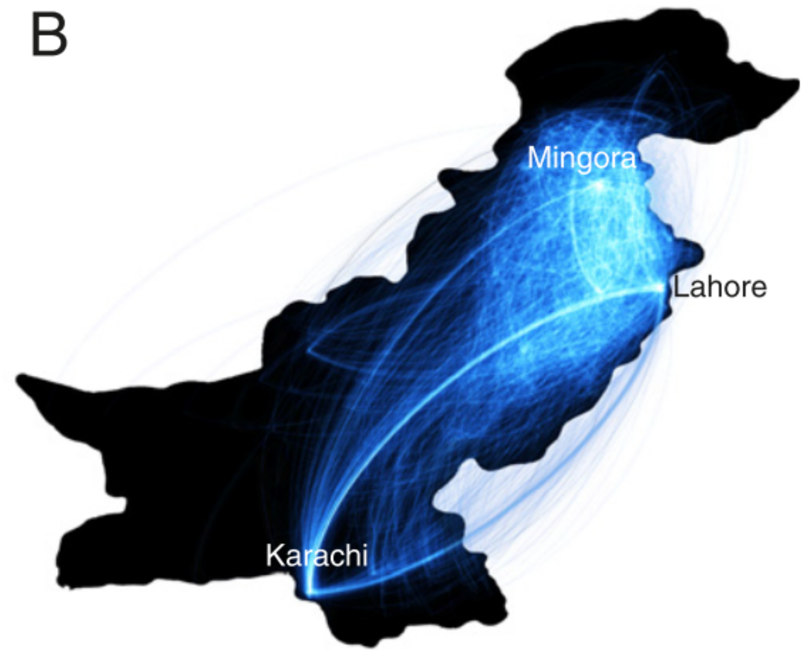
Dengue in Pakistan

- First confirmed case in 1994 in Karachi
- Prior to 2008, majority of cases were in Karachi
- Since then dengue has been spreading to other regions. (Lahore epidemic in 2011)
- Peak season occurs in the Fall (October - November)

Populations and human movements in Pakistan



Population density and mobile phone data availability by tehsil



Travel intensity between Karachi, Lahore, and Mingora regions

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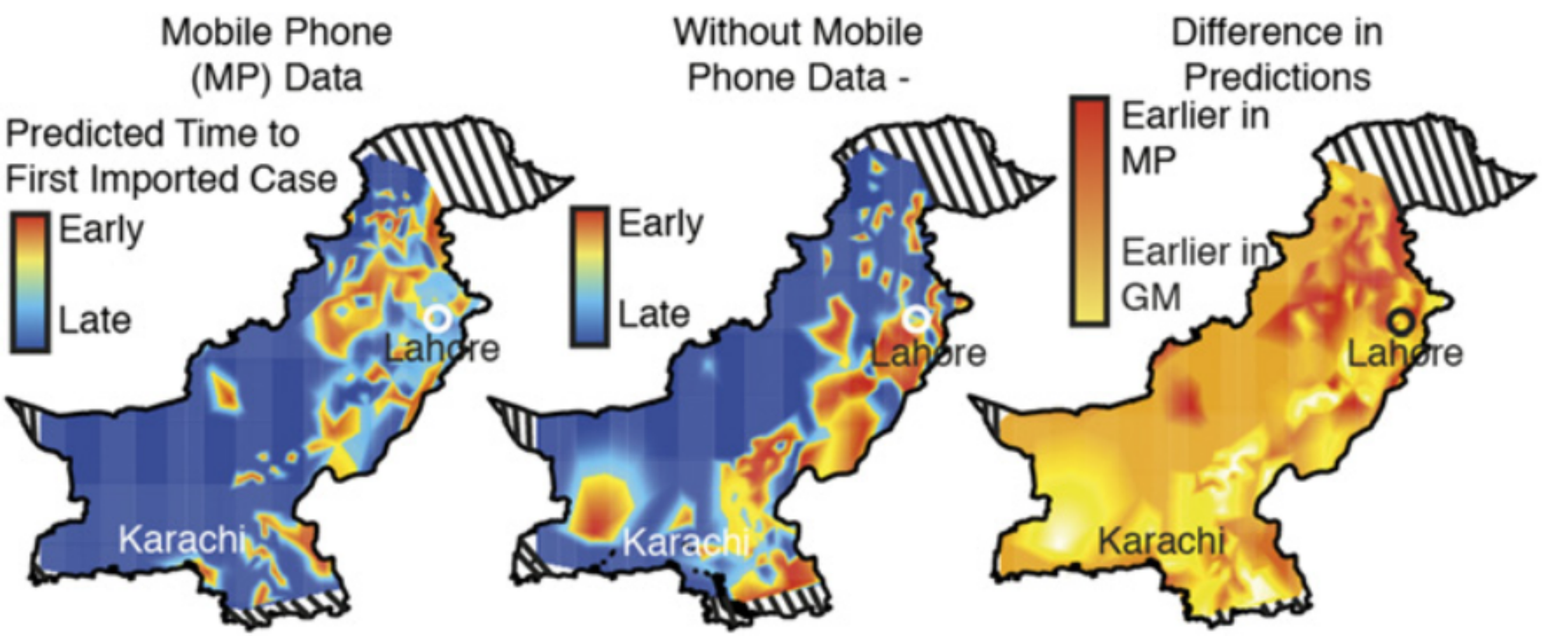
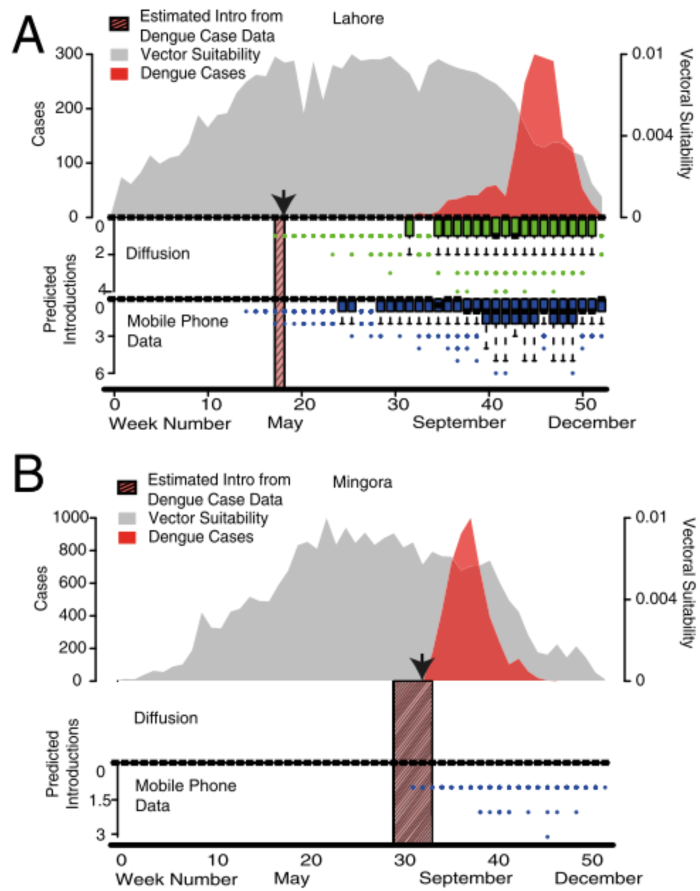
A multi-disciplinary research effort

- Collaboration between a number of research groups affiliated with,
  - Telenor Research
  - Howard T.H Chan School of Public Health
  - Center of Disease Control
  - Oxford University clinical research unit
  - Department of Zoology, University of Peshawar
  - etc.
- Lead author, Amy Weslowski, is an infectious disease epidemiologist with previous experience on utilizing mobile network data for epidemiological purposes

Research models spatial spread of dengue with human mobility across Pakistan as the primary driver



The model predicts the timing of importation of dengue from endemic regions(Karachi) to rest



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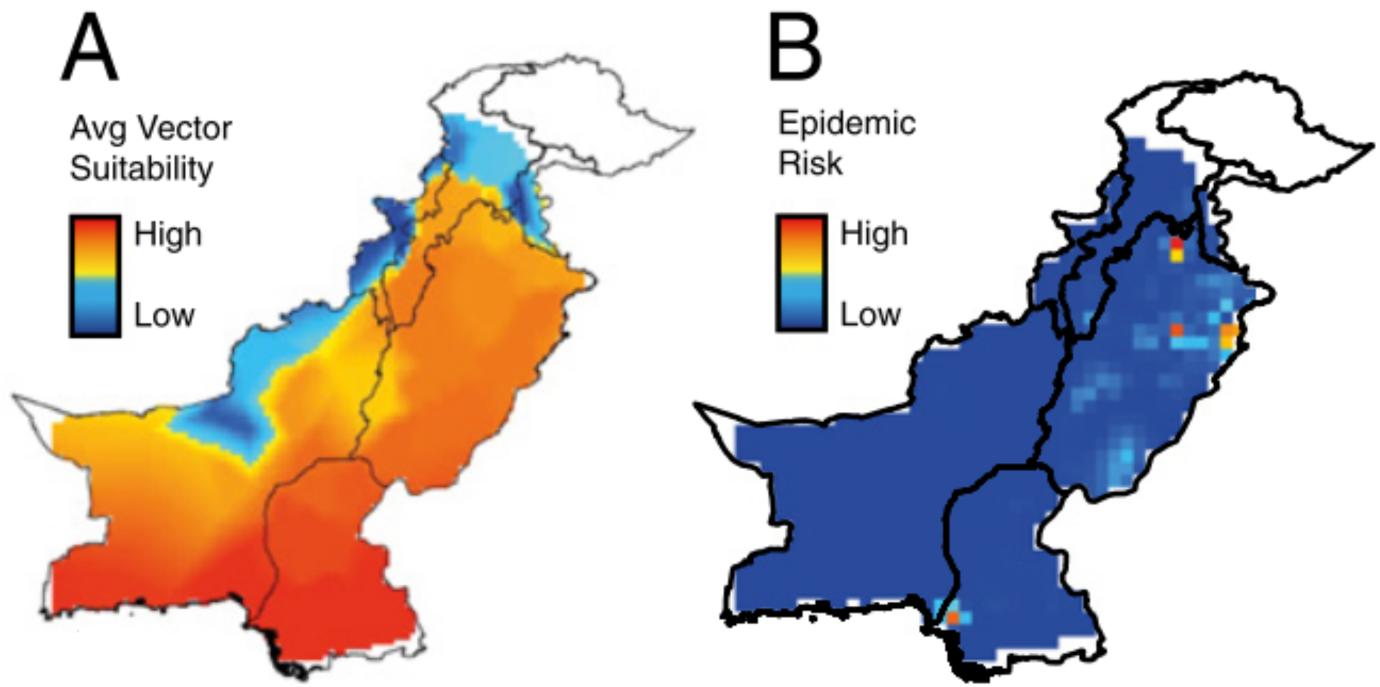
Map of epidemic risk by evaluating climate conditions and travel patterns



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Data

- Mobile phone CDR data
  - 7 months of CDR data from Telenor Pakistan from June to December of 2013 (~40 million SIMs)
  - On average 28 million SIMs active daily with 15 million SIMs generating outgoing calls with location data
  - Coverage of 352 of 388 tehsils of sub-districts in Pakistan

- Dengue data
  - De-identified daily dengue counts aggregated to the tehsils or sub-districts

Data…

- Population data
  - Up to date population estimates at the tehsil level from worldpop.co.uk

- Climate data
  - Temperature & relative humidity based on temperature taken from 38 weather stations across Pakistan

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A clear distinction is made between endemic and naive regions

- Karachi and sorrounding regions in the south of the country were identified as being endemic regions
- All other regions are assumed to be naive.
- The analysis in particular focuses on the northern regions of Lahore and Mingora in part to evaluate the effectiveness of this assumption
- Given a 2011 epidemic, Lahore was likely to have built up immunity and a limited dengue mosquito population by 2013
- Mingora was effectively a naive region in 2013

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An existing ento-epidemiological model was used to model disease dynamics in localized regions

- The model uses two sets of rate or differential equations to model human and dengue mosquito population dynamics
- Human population dynamics
  - Susceptible -> Exposed -> Infected -> Recovered
  - At the start the entire population is considered immunologically naïve (i.e. susceptible)
  - The existence of multiple strains of the disease is ignored
  - Re-infection is ignored (follows from ignoring multiple strains)

An existing ento-epidemiological model…

- Dengue mosquito population dynamics
  - Susceptible -> Exposed -> Infected
  - Elements of the life-cycle of the mosquito is incorporated
    (Aquatic -> Adult)
  - Oviposition rate (egg laying rate)
  - carrying capacity or sustainable mosquito population for a region limits
- Model constants such initial mosquito populations and host-vector incidence rates are derived from temperature based formulae
- Other constants such as the sustainable mosquito population, biting rate and reporting rates were estimated using sensitivity analysis

The use of the model is twofold

- Model is fit to the endemic region of Karachi starting at Day 1, to estimate daily infected number of people over time based on reported cases
  - Used estimate likelihood of dengue importation from Karachi to other regions on a given day

- Model is fit (in reverse) to naïve regions to estimate the time introduction of dengue from outside solely with reported cases.
  - Used to validate estimates of dengue introduction based on human mobility patterns

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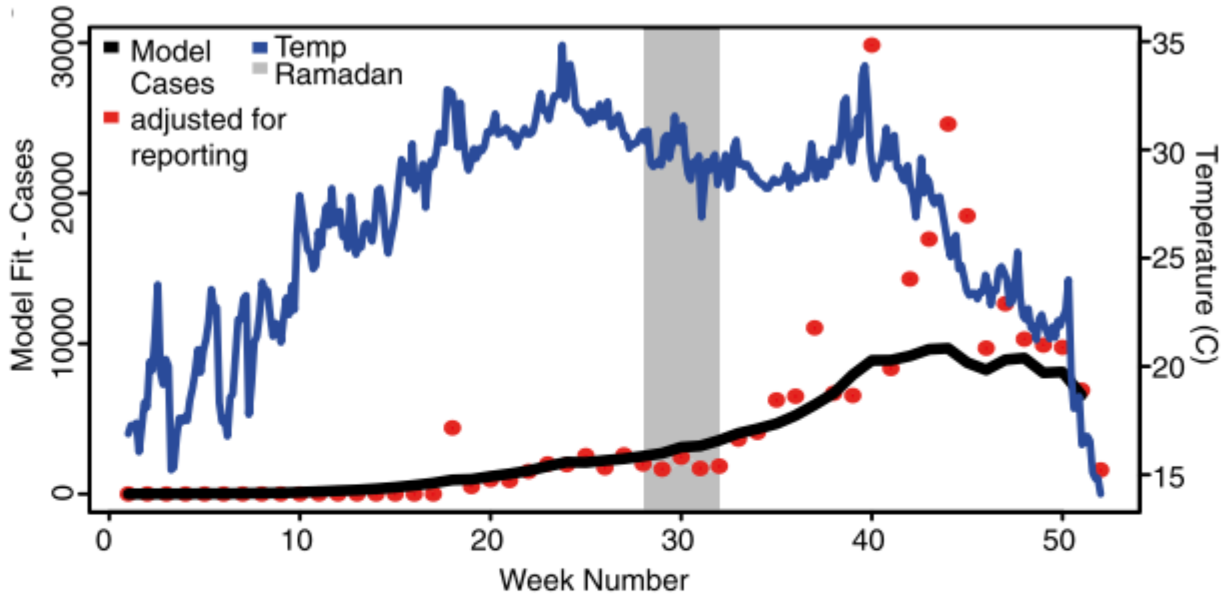

Weekly reported and estimated dengue cases in Karachi

Reporting rate, ρ	Mingora, estimated T_0	Lahore, estimated T_0
0.03	210	124
0.06	221	130
0.1	228	130
0.3	231	130
0.5	231	130
0.6	231	130
0.7	231	130
0.8	231	130
0.9	231	130

Estimated date of introduction of dengue to Mingora and Lahore using the ento-epidemiological model and reported cases

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Theoretical model

$$\frac{dS_h}{dt} = -\lambda^{v\to h}$$

$$\frac{dE_h}{dt} = \lambda^{v\to h} - \gamma^h E_h$$

$$\frac{dI_h}{dt} = \gamma^h E_h - \sigma^h I^h$$

$$\frac{dR_h}{dt} = \sigma^h I_h$$

$$N = S_h + E_h + I_h + R_h.$$

human population dynamics

- N - Susceptible human population
- E_h - Exposed individuals
- $\lambda^{v\to h}$ – vector to human incidence rate
- $1/\gamma^h$ - mean incubation period (days)
- I^h - Infected individuals
- $1/\sigma^h$ - mean duration of infection
- R_h - Recovered individuals

$$\frac{dA}{dt} = \theta_A\left(1 - \frac{A}{K}\right)V - (\epsilon_A + \mu_A^V)A$$

$$\frac{dS_V}{dt} = \epsilon_A A - \lambda^{h\to V} - \mu_V^V S_V$$

$$\frac{dE_V}{dt} = \lambda^{h\to V} - \gamma_V^V E_V - \mu_V^V E_V$$

$$\frac{dI_v}{dt} = \gamma_V E_V - \mu_V^V E_v$$

$$V = S_v + E_V + I_V.$$

mosquito population dynamics

- A - early stage mosquito population
- V - Adult mosquito population
- S_v - Susceptible mosquitoes
- E_v - Incubating mosquitoes
- $1/\gamma^v$ - mean incubation period (days)
- $\lambda^{h\to v}$ – human to vector incidence rate
- I_v - Infected mosquitoes
- ε_A - rate of progression to maturity
- $\mu^A{}_V$ - mortality rate of early stage mosquitoes
- $\mu^V{}_V$ - mortality rate of adult mosquitoes
- K - sustainable maximum mosquito population

Estimating host-vector incidence rates and transmission probabilities

$$\lambda^{V \to h} = \frac{a\,\phi^{V \to h} I_V S_h}{N_h}$$

$$\lambda^{h \to V} = \frac{a\,\phi^{h \to V} I_h S_V}{N_h},$$

$$\phi^{h \to V}(T) = 1.044 \times 10^{-3} T \times (T - 12.286) \times (32.461 - T)^{1/2}$$

$$\phi^{v \to h}(T) = 0.0729T - 0.97.$$

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Estimating temperature driven constants of the dengue mosquito life cycle

$$\epsilon_A^V(T) = 0.131 - 0.05723T + 0.01164T^2 - 0.001341T^3 + 0.00008723T^4 - 3.017\times10^{-6}T^5 + 5.153\times10^{-8}T^6 - 3.42\times10^{-10}T^7$$

$$\mu_A^V(T) = 2.13 - 0.3787T + 0.02457T^2 - 6.778\times10^{-4}T^3 + 6.794\times10^{-6}T^4$$

$$\mu_V^V(T) = \mathrm{RHF}(T, \mathrm{RH}) * \left(0.8692 - 0.1599T + 0.01116T^2 - 3.408\times10^{-4}T^3 + 3.809\times10^{-6}T^4\right)$$

$$\theta_V^V(T) = -5.4 + 1.8T - 0.2124T^2 + 0.01015T^3 - 1.515\times10^{-4}T^4$$

$$\gamma_V^V(T) = \frac{(3.3589\times10^{-3}T_k)/298\times\exp((1{,}500/R)(1/298 - 1/T_k))}{1 + \exp((6.203\times10^{21})/R(1/(-2.176\times10^{30}) - 1/T_k))},$$

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Country wide travel patterns are extracted from CDR

- For each day, each subscriber in the data is assigned to the his/her most frequently observed mobile phone tower
- Travel is estimated each day between mobile phone towers by considering a subscriber's location w.r.t their location the previous day
- Movements are aggregated at the tehsil level based on the origin and destination and normalized by the number of active subscribers in the origin tehsil(flux)
- Movement estimates for the period 1st January to 1st June were generated by assuming the same mean number of normalized number of trips and adding noise

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Predicting importation of dengue to naive regions from endemic regions through travel

- Approximately 30% of the subscribers in Karachi traveled outside daily (β)
- The model provides a daily estimate of number of infected hosts in Karachi (m_t)
- Naïve estimate of infected travelers: $m_t \beta$
- β is varied between 10%,20% and 30% in simulations, to account for uncertainty and likelihood of overestimating travel with CDR

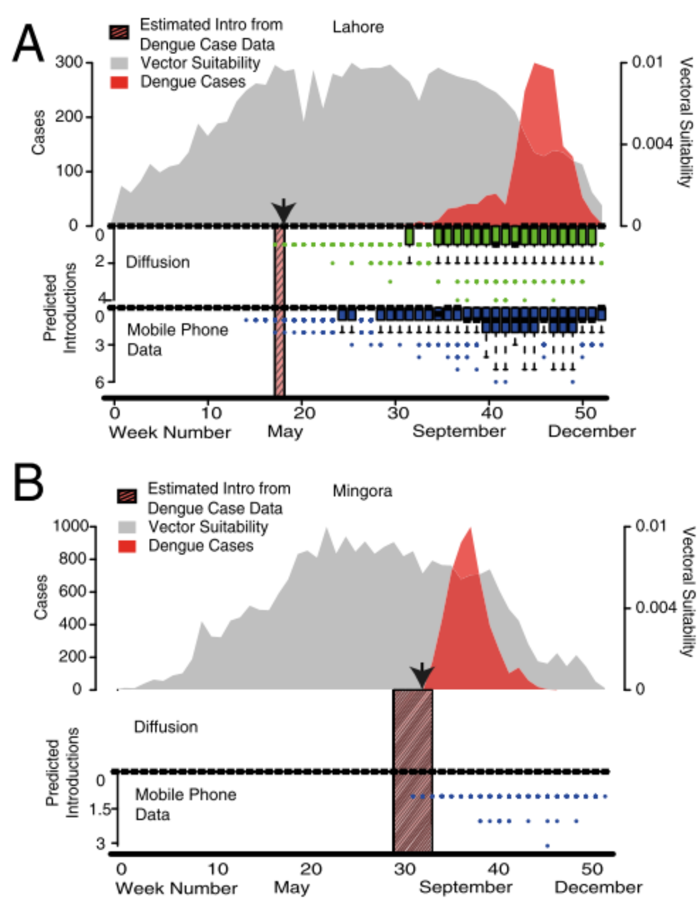
Predicting importation of dengue to naive regions…

- Estimated infected travelers are apportioned to destination tehsils based on the percentage of estimated travel to those destinations
- The state of infection of an 'infected' host is a spectrum due to viral dynamics. This affects transmission likelihood when bitten
  - Viral dynamics are not dealt with directly
  - Instead simulations are done using probabilities transmission sampled from a series of binomial distributions with different fixed probabilities (0.01 to 0.9)

Predicting importation of dengue to naive regions…

- 200 simulation done for each combination of the fraction of Karachi population traveling outside and the fixed transmission probability
- The most likely date of first case of imported dengue at the destinations is estimated from results of the simulations
- Estimates predominantly affected by the number of people traveling out from Karachi and is not very sensitive to transmission probability

Estimates demonstrate accuracy of model but also the effect of prior epidemics and immunity



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A map of dengue epidemic risk was developed for Pakistan by combining climatic suitability and mobility patterns

$$risk_{epidemic}(X) = \sum_{t=1}^{N} Z_X(T_t)\, Y_{X,t}$$

Where,

Z_X – *Vector suitability at location X*

T_t – *temperature at X at time t*

$Y_{X,t}$ – *the number infected travelers*

Environment suitability for dengue mosquitoes is driven by temperature

$$Z_X(T) = \exp(-\mu_V^V(T)\gamma_V^V(T))/\mu_V^V(T)^2$$

Where,

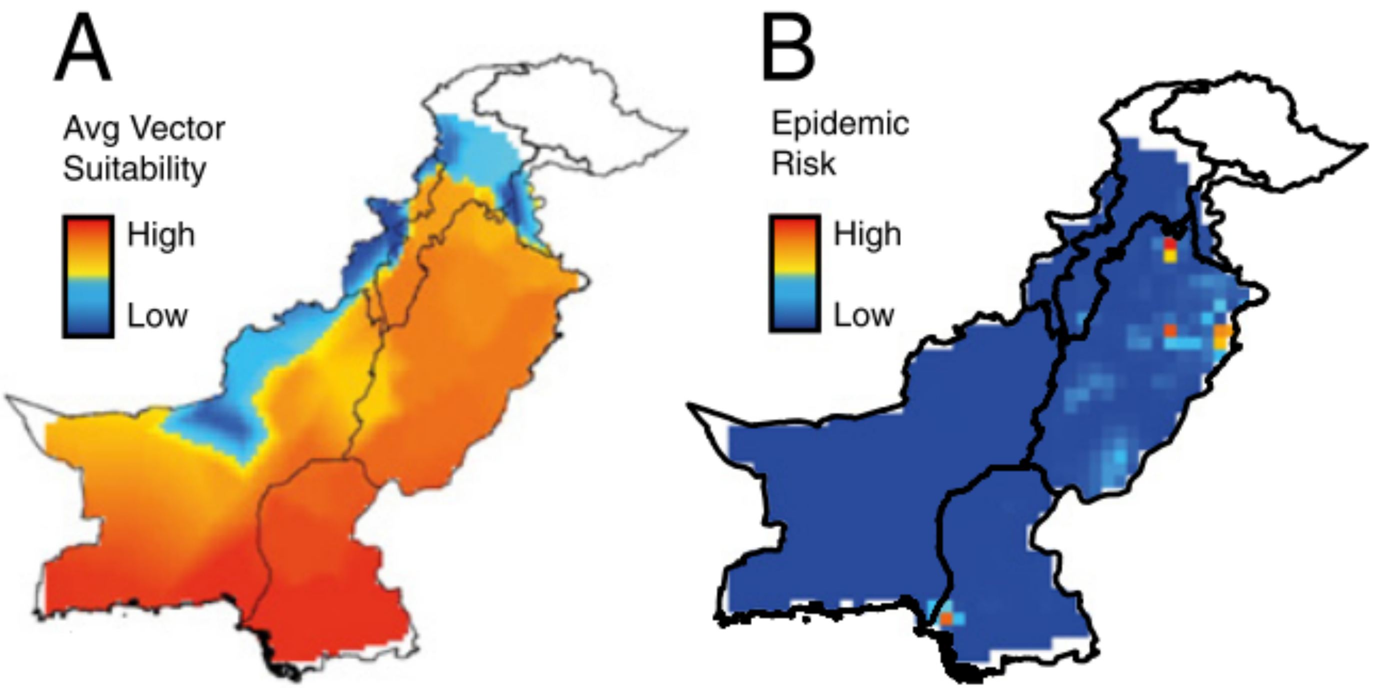
T – *temperature*

$Z_X(T)$ – *Suitability at X*

μ_V^V – *instantaneous death rate of adult female mosquitoes*

γ_V^V – *incubation period of dengue*

Epidemic risk is dominated by importation through travel



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Research highlights potential value of human mobility estimates, but is not without issues

- There is a disconnect between the epidemiological model and the prediction of dengue introduction through travel
- Ignores existence of disease serotypes (strains)
- Ignores history of dengue in the region and immunological covariates
- Validity and alignment of temperature based expressions for entomological properties for dengue in a local context
- Multiple parameters estimated through brute force search (traveler percentage, mosquito carrying capacity, biting rate etc.)

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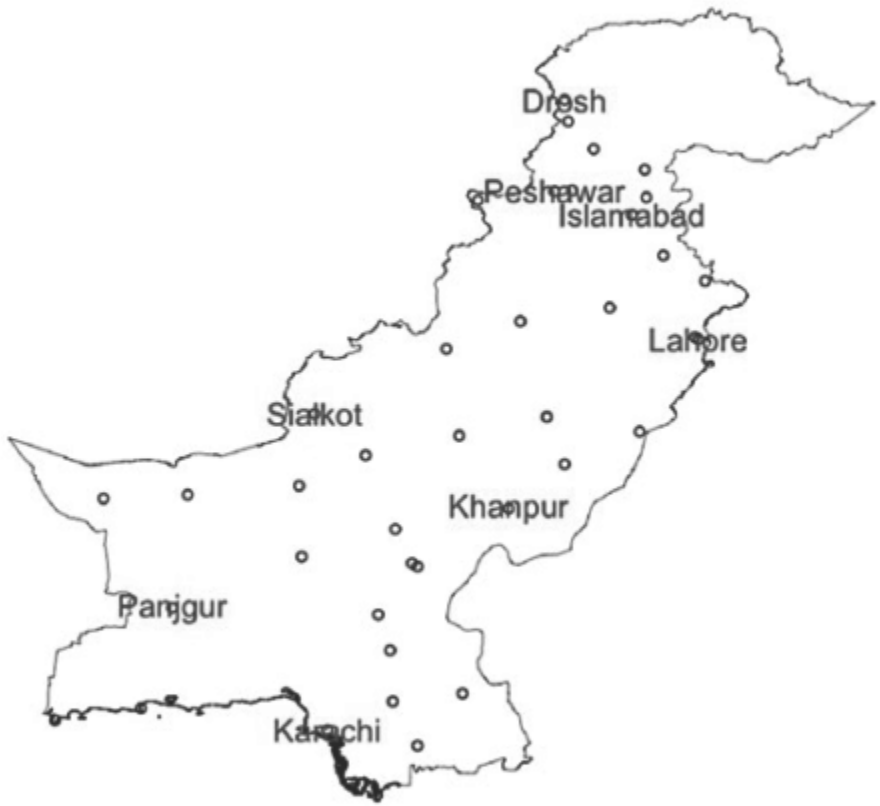
Issues…

- Relatively low spatial sampling of weather data (38 weather stations, Pakistan is about 14 times Sri Lanka in area)
- Differences between air and water temperatures (also microclimates?)

Placement of weather data used in the research



Key data and parameters that may determine the success of similar work in Sri Lanka

- Unit of spatial analysis- (MoH region, base station coverage region, DSD ?)
- Accurate spatio-temporal data on reported dengue cases (daily?)
- Reporting rate (~100% in SL?)
- Regional dengue populations
- Regional serotype prevalence
- Regional immunological data/historical case serotypes
- Entomological parameters acceptable for the region
- Spatiotemporal information on preventive measures?

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