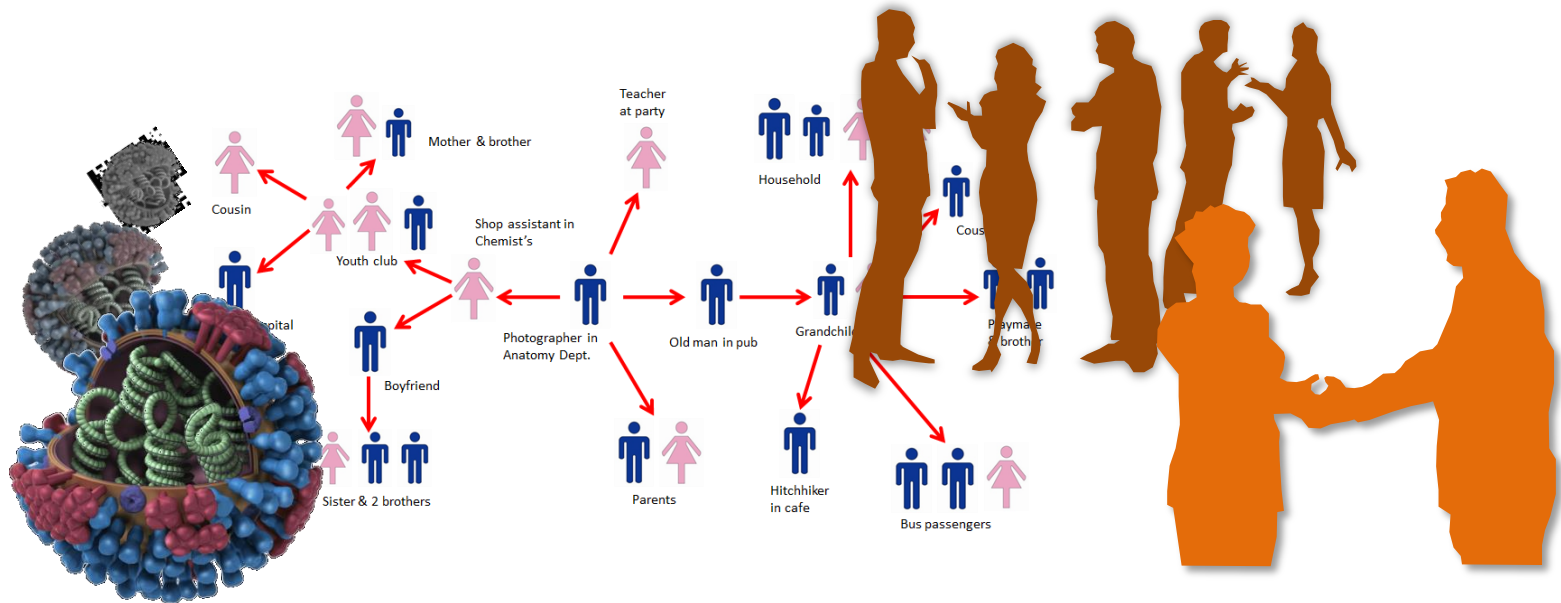
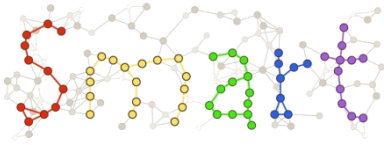


Relating human contact patterns to influenza infection

Understanding the host ecology of human influenza



Jonathan Read
Epidemiology and Population Health



FLUSCAPE 流感景观
Immunological Landscapes of Influenza in China 在中国的流感免疫景观



Outline

Motivation

SMART study

School-based and social interaction patterns

PCR-detected infection with influenza and other respiratory viral pathogens

FluScape study

Social connectivity

Antibody titres to historic influenza strains

Hong Kong pandemic flu study

Social encounters

Paired serology; antibody titres

Conclusions

1. MOTIVATION

- Central tenet of epidemiology:
 - Transmission of many respiratory pathogens (including influenza) depends on close contact and/or co-location of hosts
- Basis of interventions:
 - Quarantine
 - Contact tracing
 - Social distancing
- Connectivity drives epidemics

1. MOTIVATION

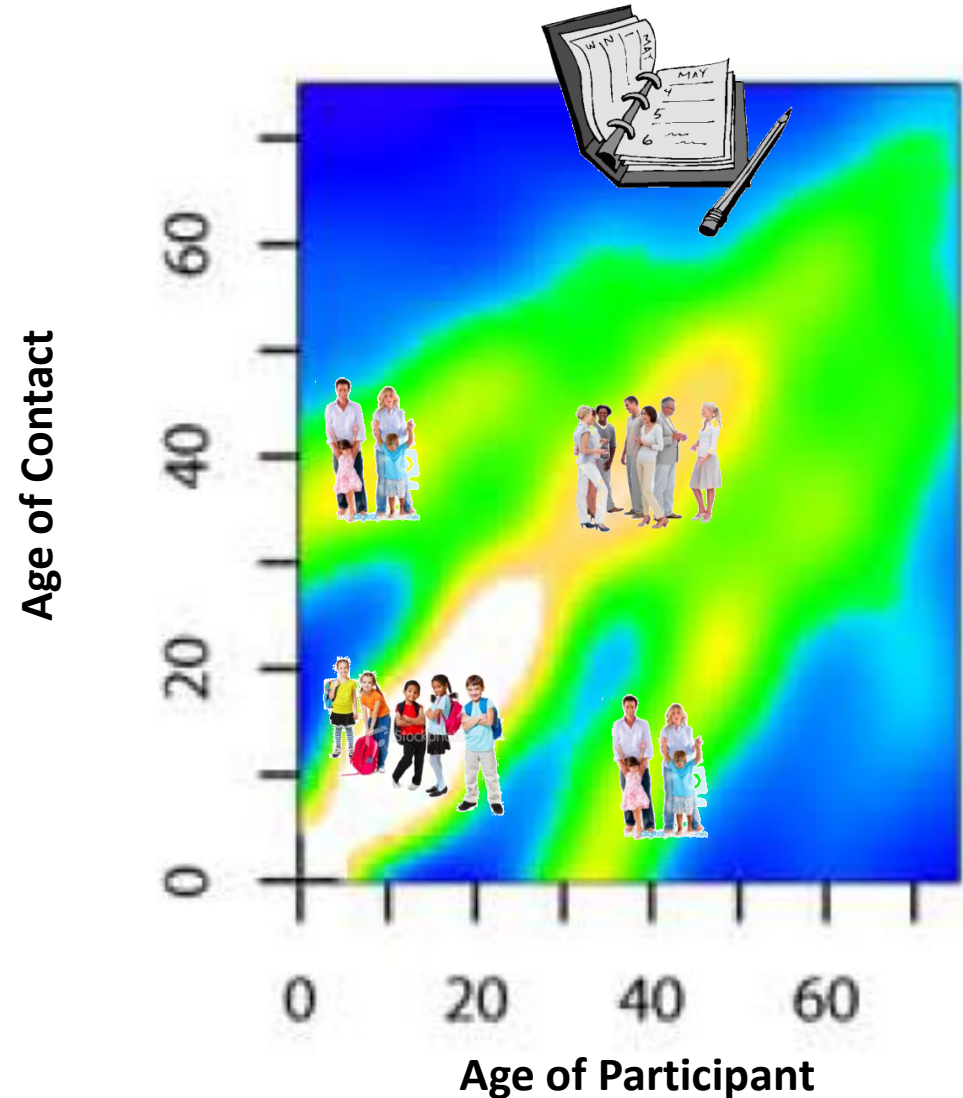
- Evidence that contact is important for transmission?
 - Quarantine seems to work
 - Contact tracing seems to work
 - Social distancing works??
 - Models with contact-driven transmission as assumption can work
- Direct evidence?
 - Limited; handful of small studies

Social mixing patterns

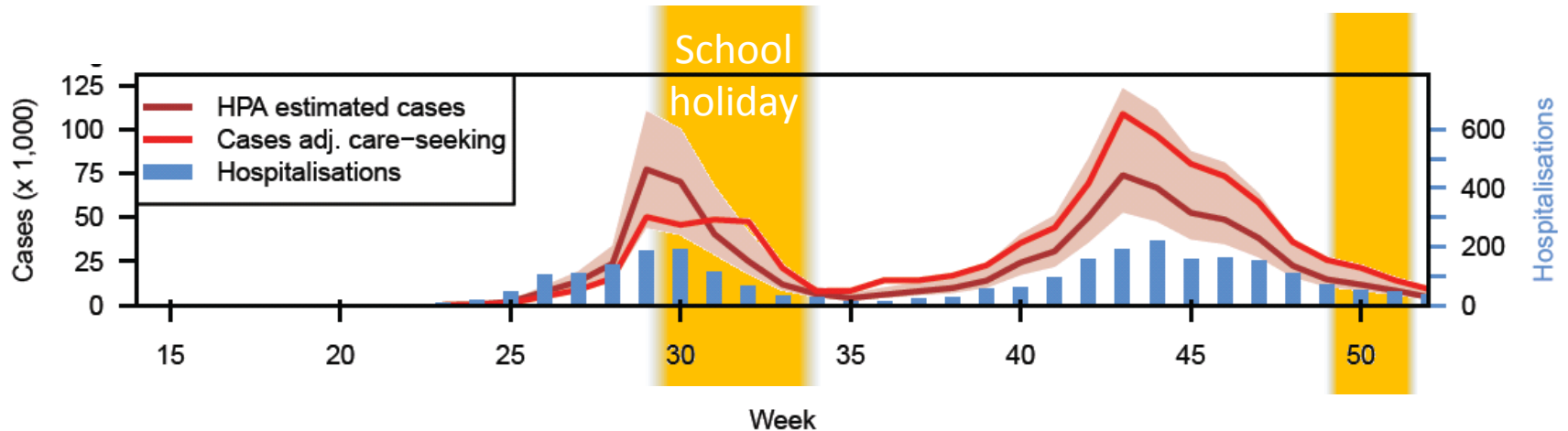
Until recently, social contact patterns were unquantified

Polymod study

- 7,290 participants
- Focussed on age-mixing patterns
- Found strong assortativity by age
- Children have highest contact rate
 - mostly with other children and parents



2009 A/H1N1 pandemic UK



- Reduced mixing of school-age children in summer holiday thought to have slowed pandemic
- Epidemic growth renewed after holiday period

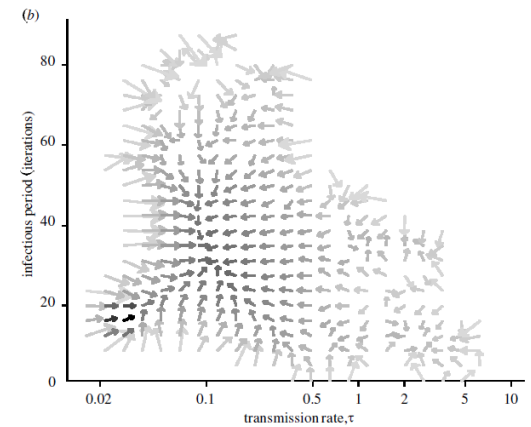
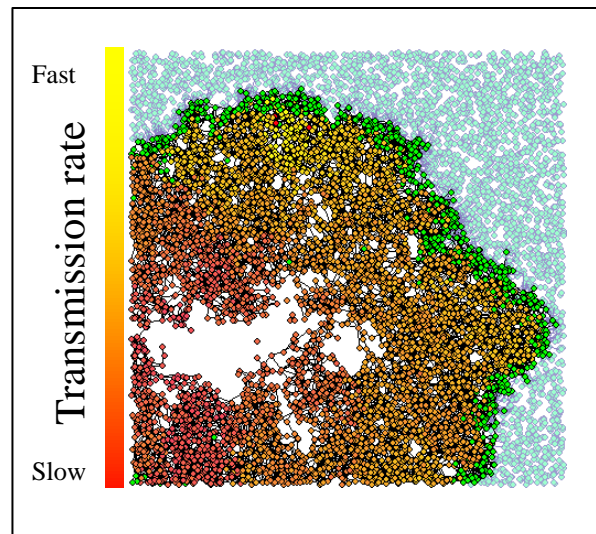
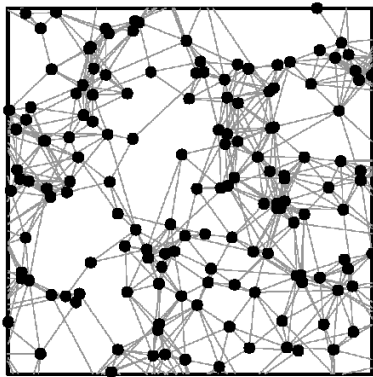
Source: HPA, FluSurvey

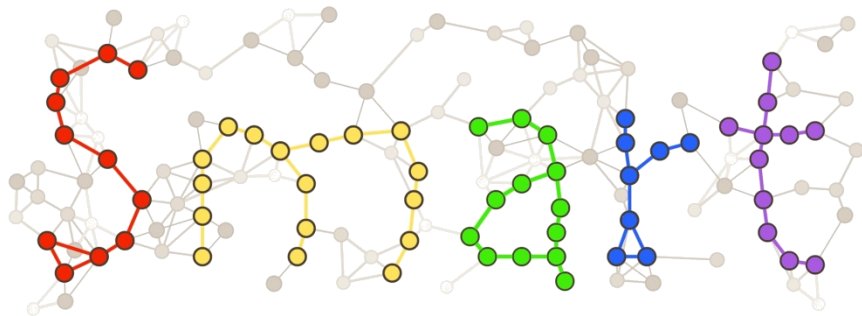
bin-Reza et al 2012 Infl Other Resp Vir in press

Stebbins et al 2011 Ped Inf Dis J, 30

1. MOTIVATION

- Network-based models of pathogen evolution





Social Mixing And Respiratory Transmission study

Pittsburgh, USA

- Aims: compare and link information on social networks to influenza infection



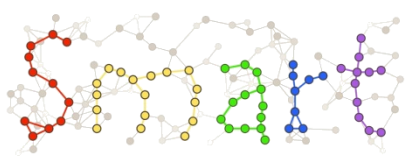
Timeline

Year 1

- Social network measurement
- Contact diaries
- Electronic proximity sensors (motes)

Year 2

- School-based surveillance of Influenza-like illness
- Detect and identify virus via PCR
- Sampled contemporaneous social network information



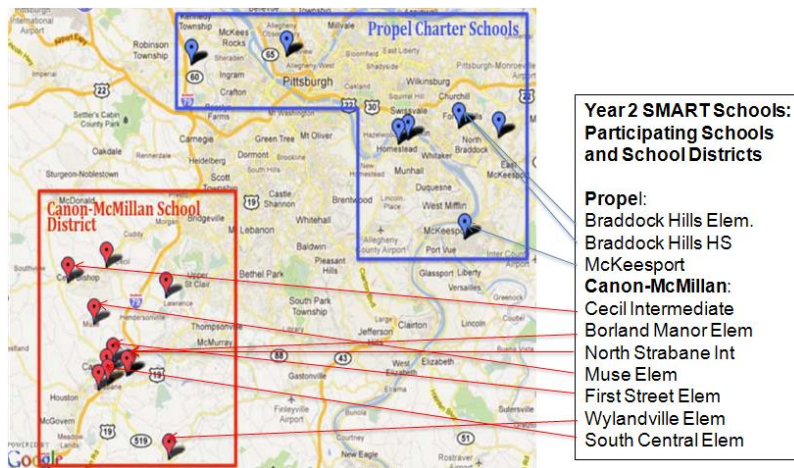
Study metrics

Study population

- 9 schools
 - 6 elementary
 - 2 intermediate/middle
 - 1 high school
- All within or around Pittsburgh and Canonsburgh, PA.

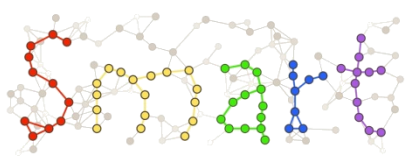
Sample size

- 2,519 students
- Study ran Dec 2012 – Mar 2013

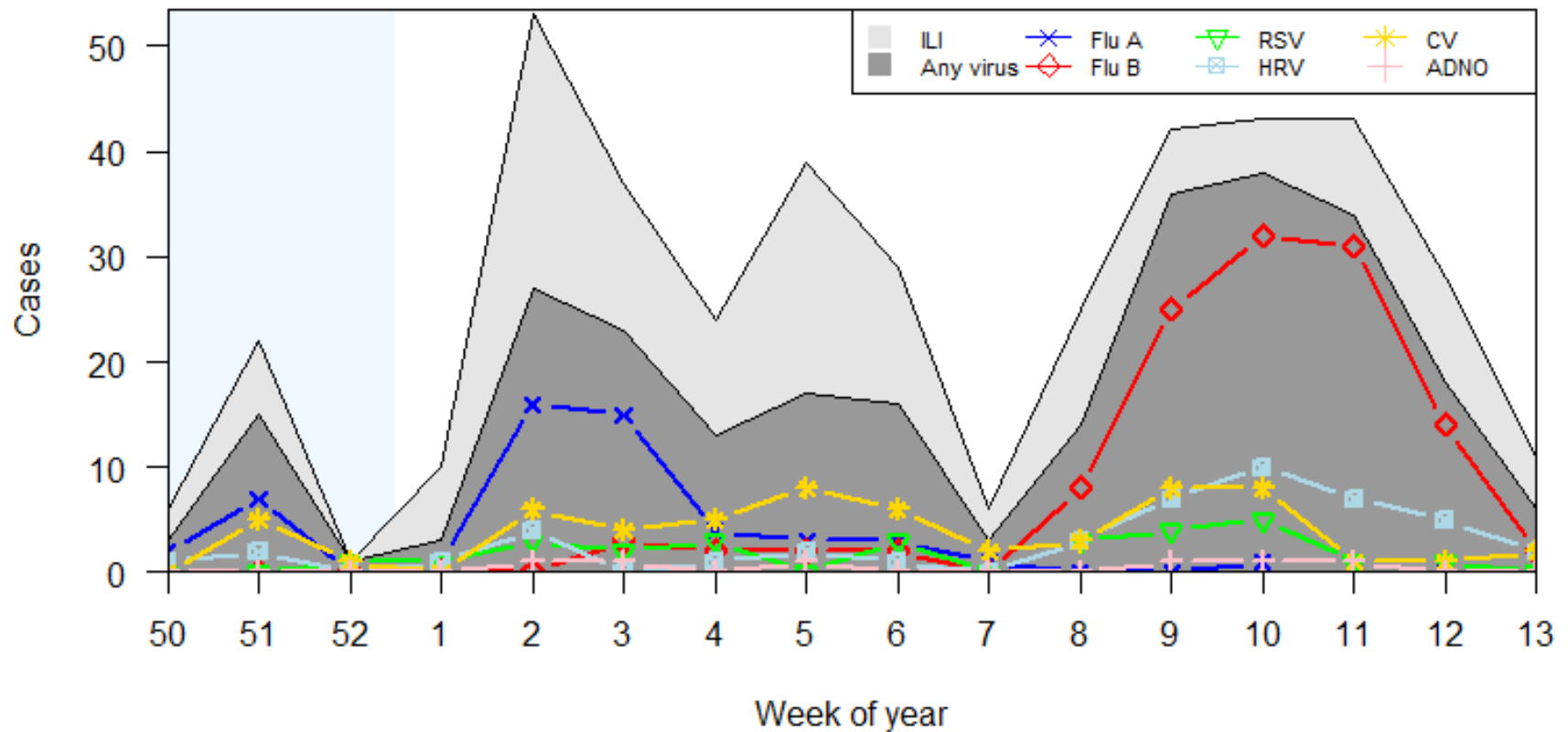


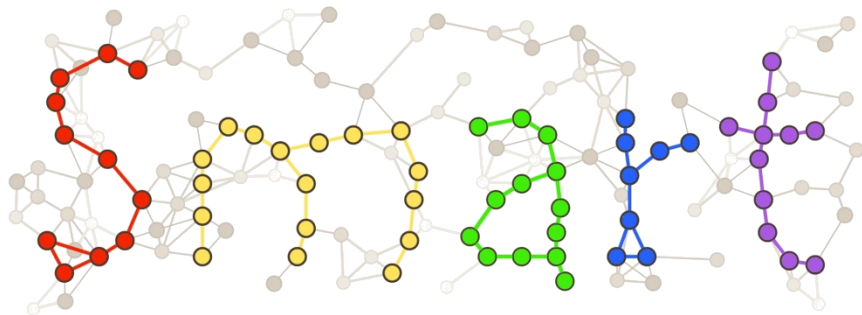
Case detection

- 408 students matched case definition (ILI) and were swabbed (a few multiple times)
- 292 swabs positive for virus
 - 57 Influenza A
 - 134 Influenza B



Year 2: School-based ILI Surveillance 2012-13





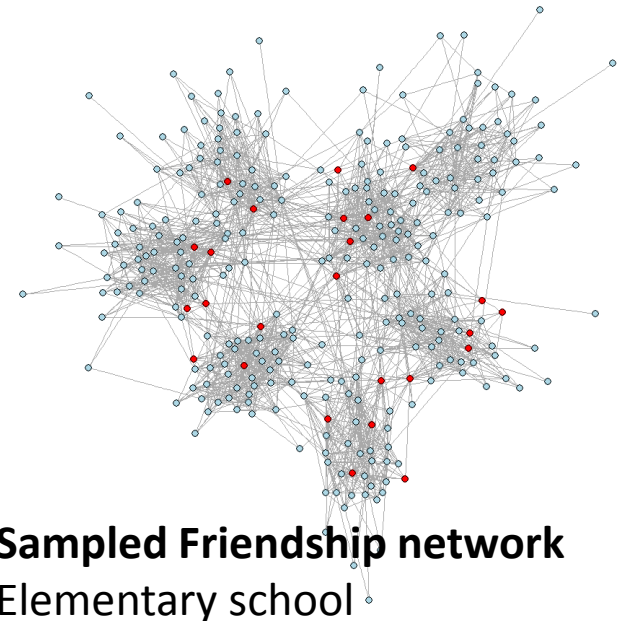
Social Mixing And Respiratory Transmission study

Summary

- Infection clustered by district, school and class
- Time spent in school associated with increased risk
 - Reduced school day potential alternative to full school closure
- Attending same class as influenza case increased risk of infection

Future work

1. Incorporate social network information
2. Partial likelihood methods / point process models (PJ Diggle)



Sampled Friendship network
Elementary school

Landscapes of influenza immunity

- Simple meta-population model
 - Density and connectivity gradient
 - stochastic transmission
 - restocking of susceptibles
- Previous infection patterns shape landscape for future epidemics



Large Urban populations



Small Rural populations

log(flu cases) in successive years n = 10 million

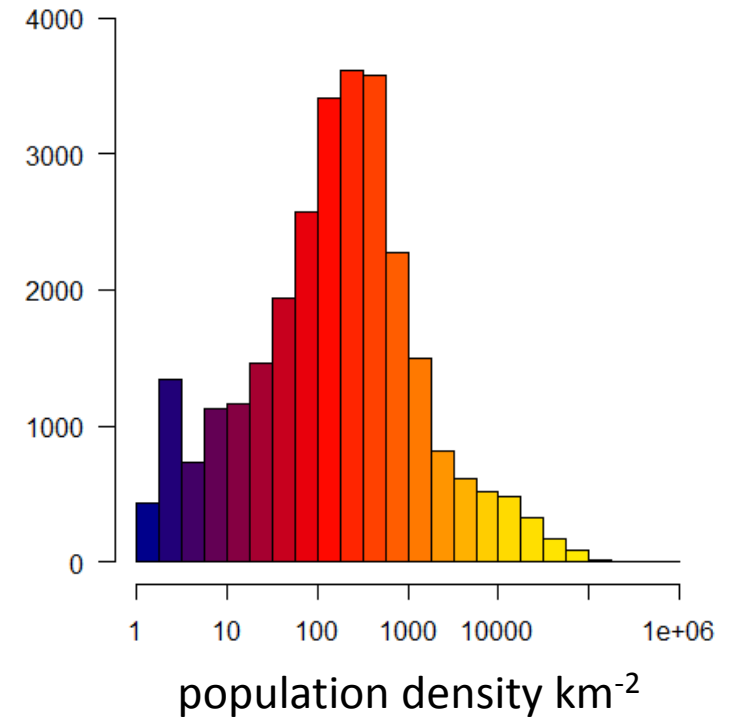
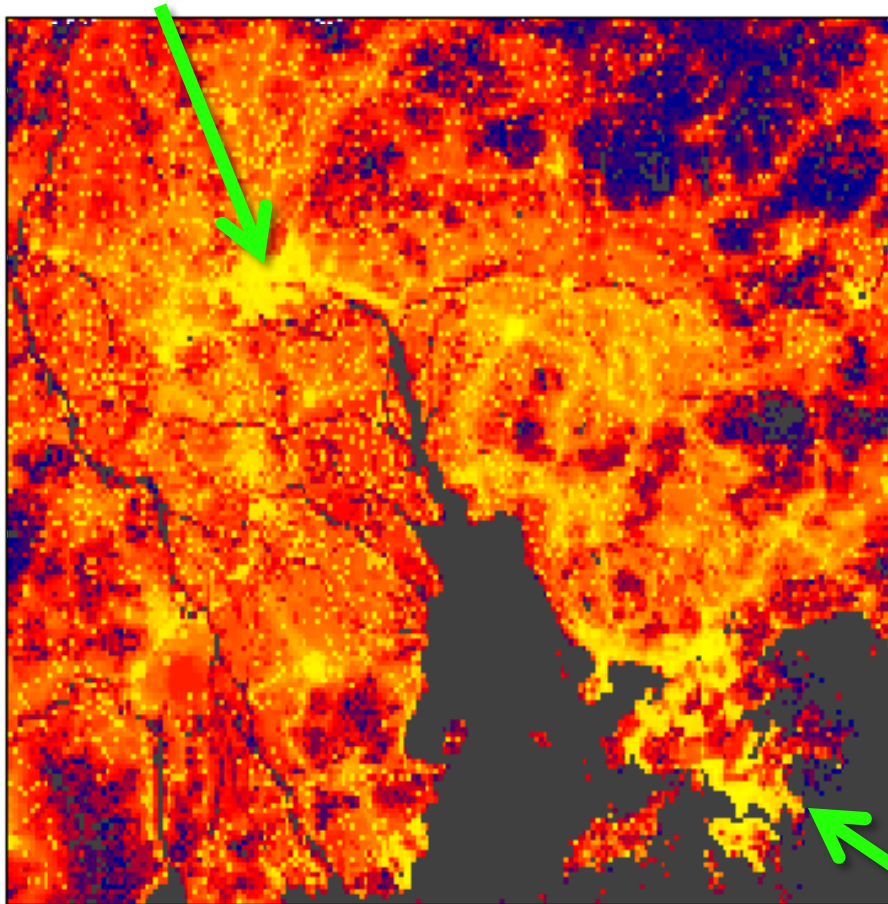


Easy to show with models
 Does it happen with real populations?

Time →

Population Density, GuangDong

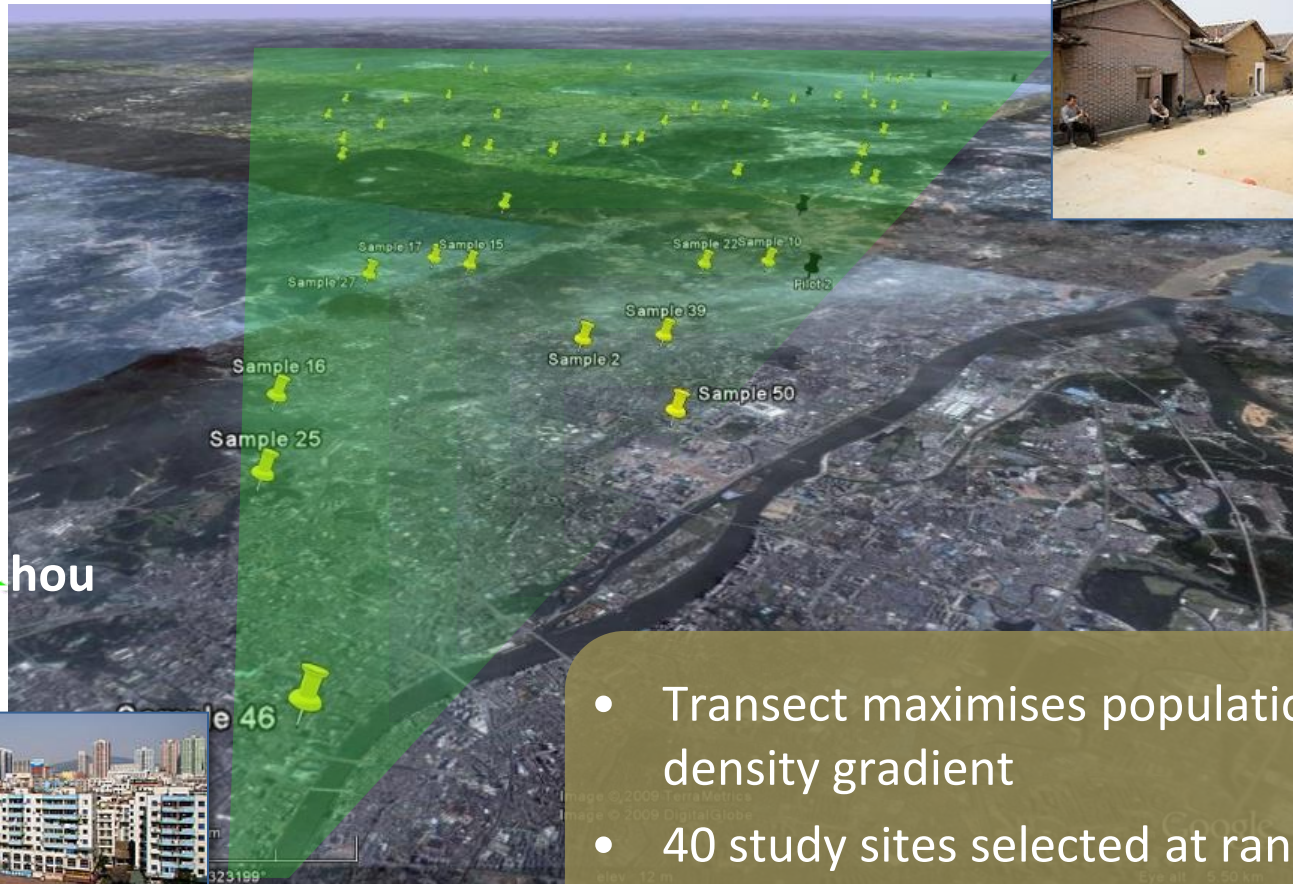
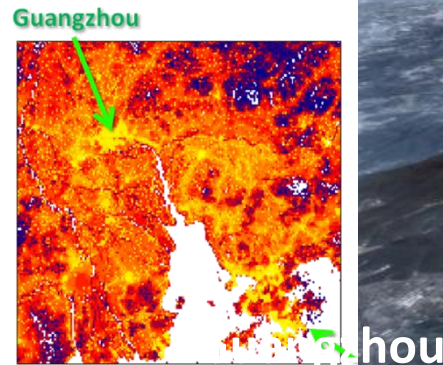
Guangzhou



Hong Kong

Log(density)

Study design



- Transect maximises population density gradient
- 40 study sites selected at random
- Recruit min. 20 household per site

Information and specimen collection

Households are sampling unit

Household questionnaire

- Demography, etc

Individual questionnaire

- Occupation
- Vaccination history and recent infections
- Contact Diary
 - Number of contacts
 - Location of contacts

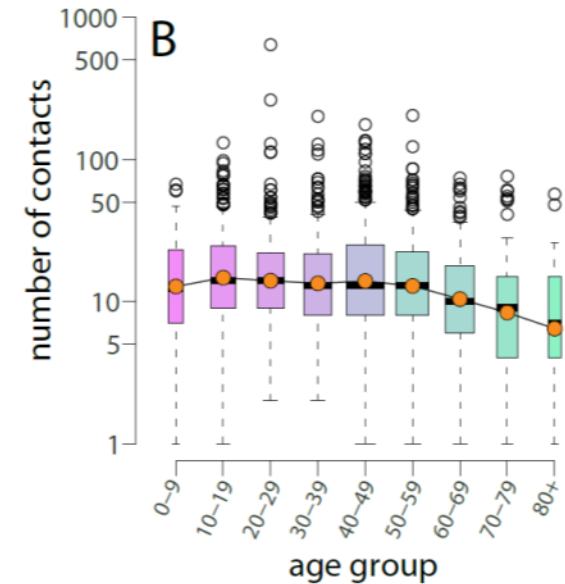
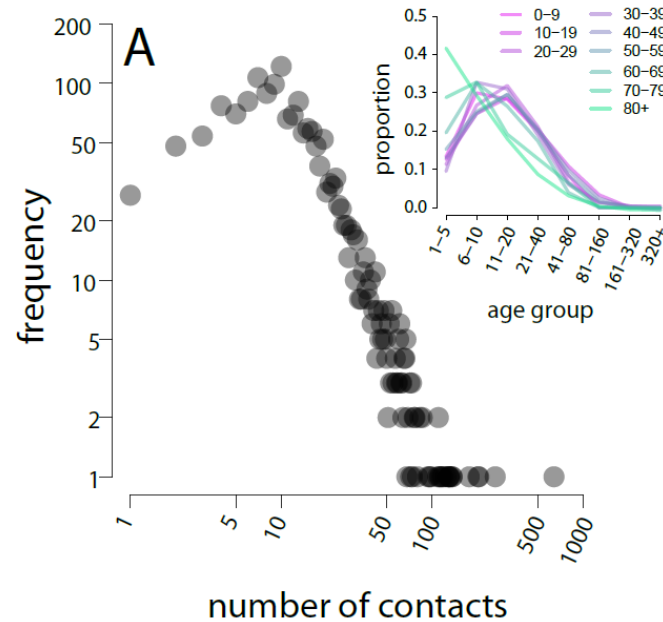


Participants = 1,838
Households = 1,019
Locations = 40



Number of contacts

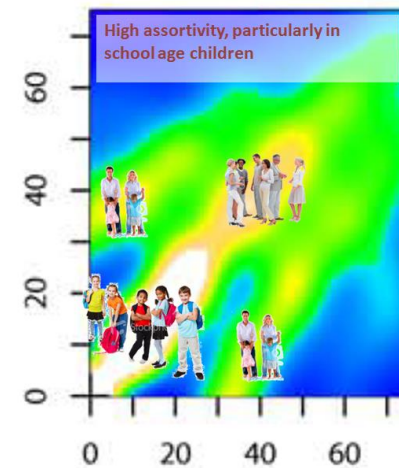
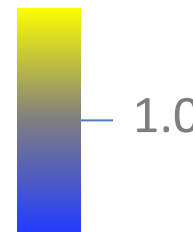
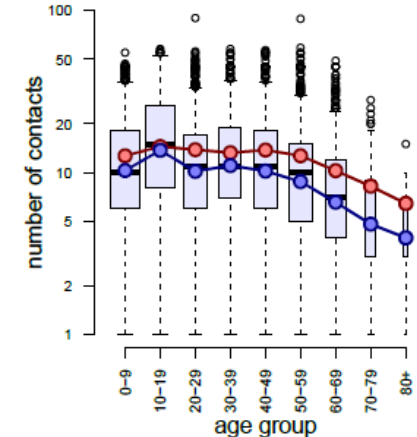
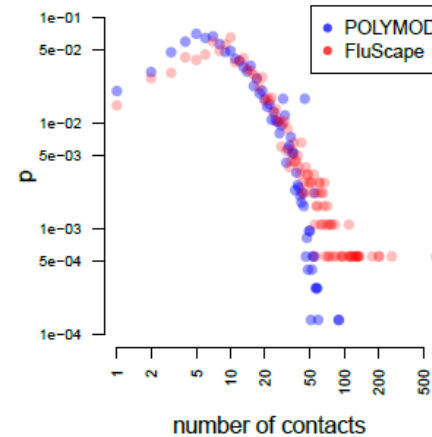
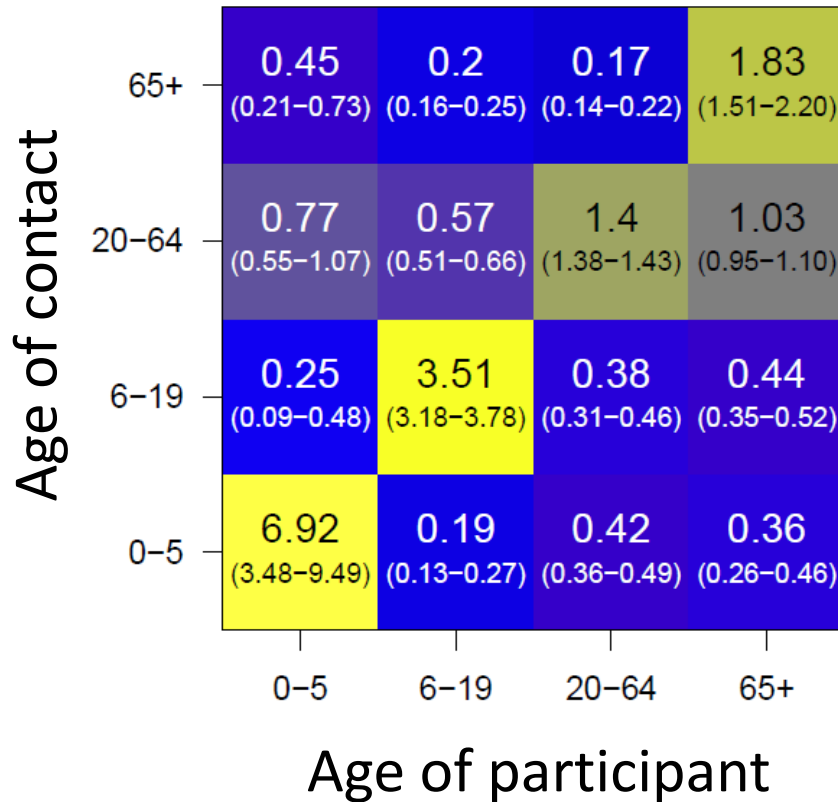
- Social contact
 - face-to-face conversation
 - skin-on-skin touch
- 1,838 participants
- 12,147 contact events
- 33,789 people encountered
- 4,803 locations (2,461 unique)



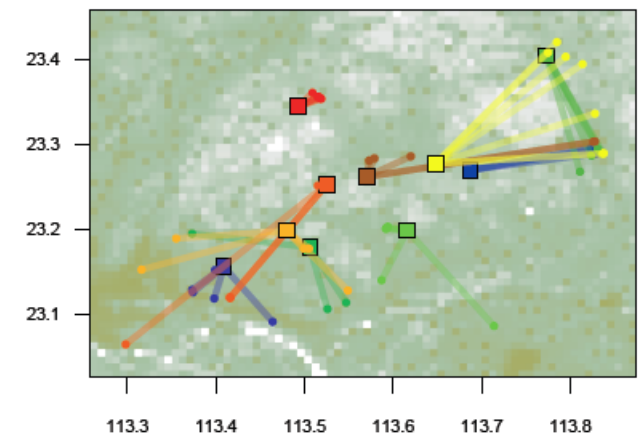
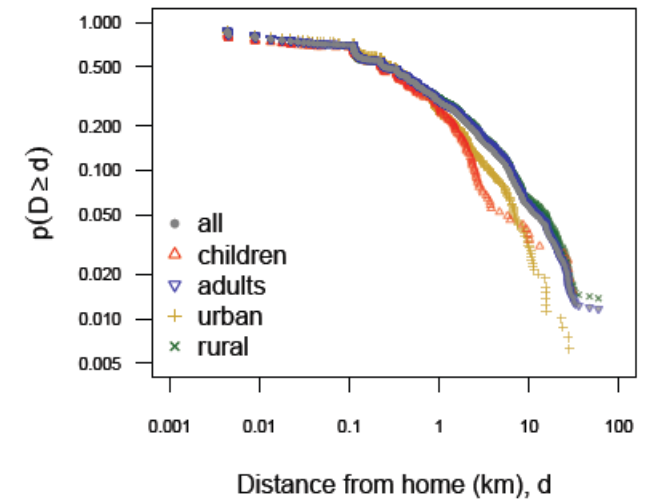
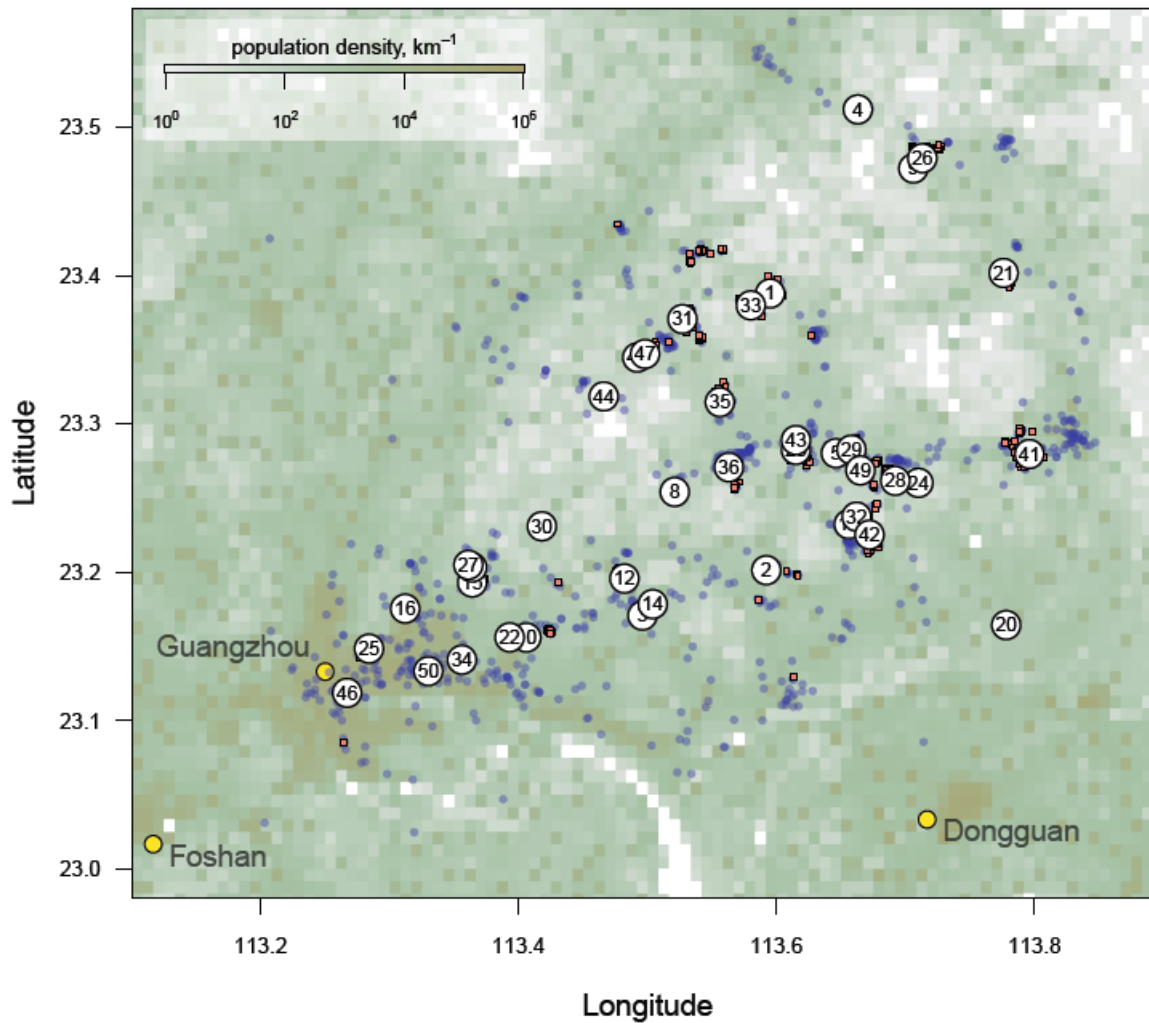
- Differences by age
- No difference between urban and rural populations

Age-based mixing patterns

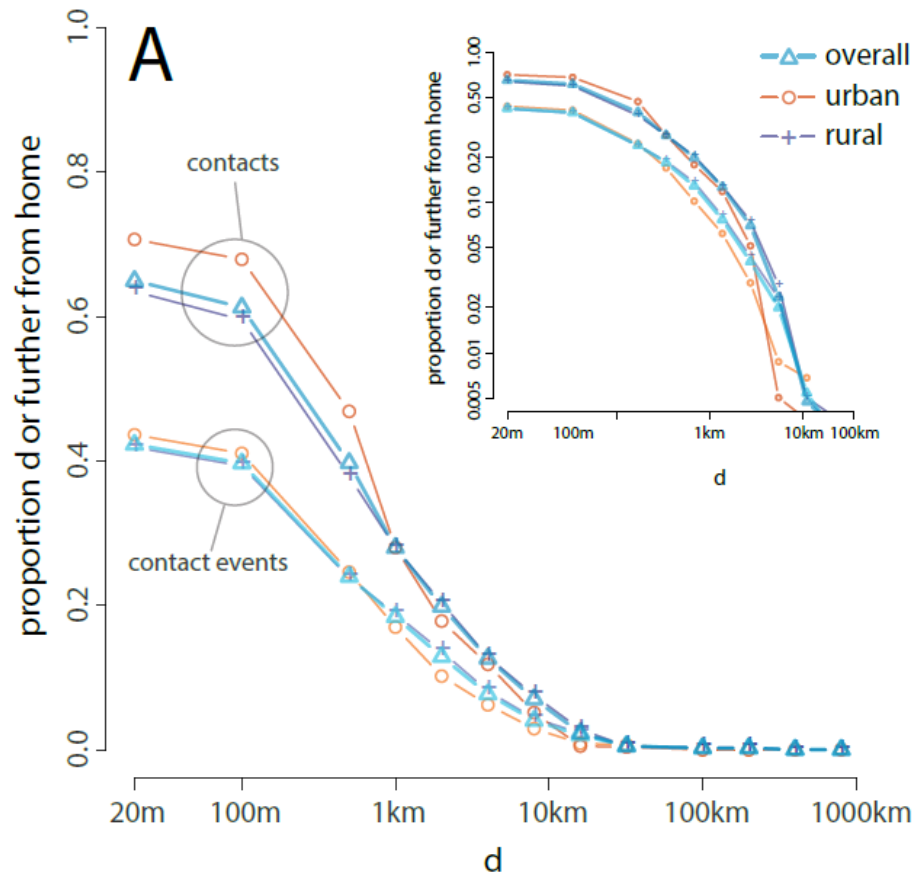
Ratio observed / expected by random mixing



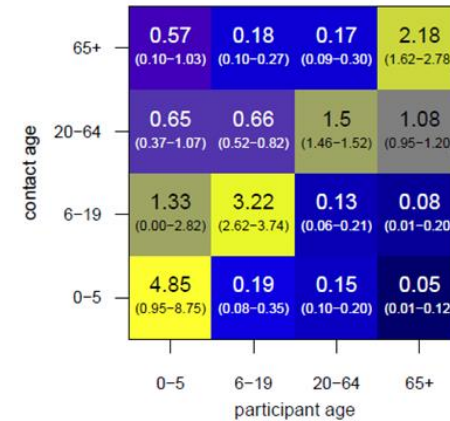
Fluscape contact locations



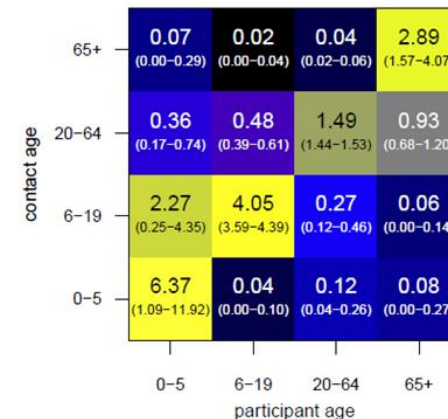
Distance from home



Not Home, <0.5km



Not Home, ≥0.5km

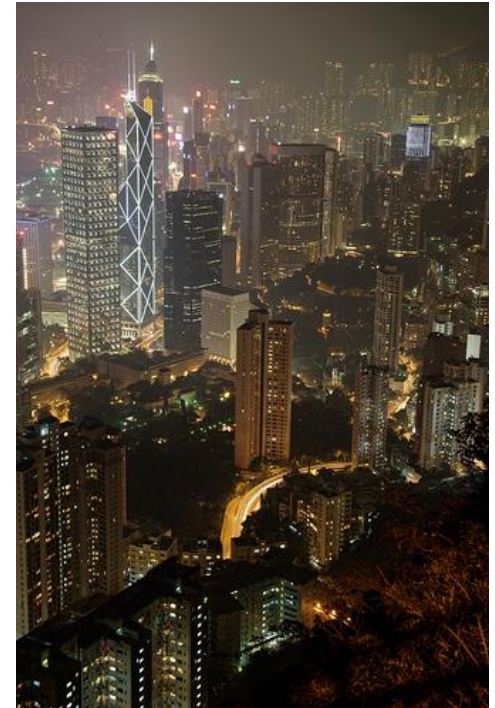


Summary

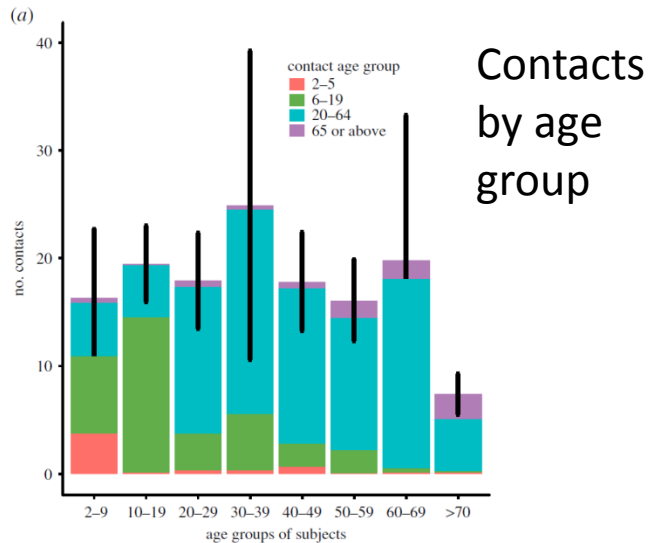
- Age plays important role in defining contact patterns
- Urban and rural populations differ by distance travelled to make contacts, but not in number of contacts
- Strong heterogeneity of influenza exposure by location
 - Individual-level contact information does NOT explain titres
- An individual's exposure to influenza appears to be defined by the local population (connectivity?)

Hong Kong Pandemic Flu study

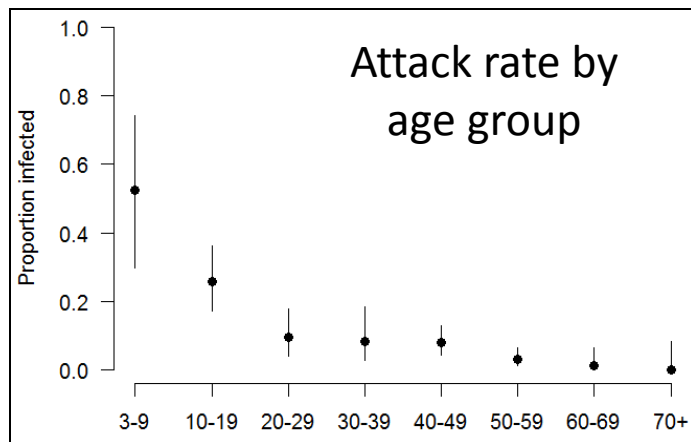
- Longitudinal study, 2009-2010
- Contact diaries collected from participants
- Paired serological samples – titre-rise to A/H1N1pdm09 confers infection
- Base-model
 - Age, child in household, district
- Candidate variables
 - 10 derived from contact diary, including number of contacts and number of locations visited
- 762 participants; 77 of whom were infected



Hong Kong Pandemic Flu study

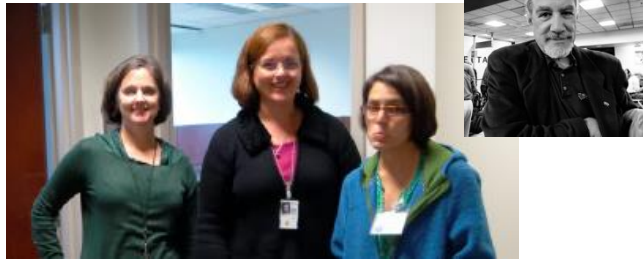
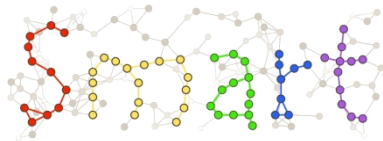


- Across range of regression models, age consistently important in explaining risk of infection
- Individual-level contact behaviour alone did not explain age-specific odds of infection
- Within age-group, number of locations and numbers of contacts increased odds of infection (approx. 10% per 10 contacts or per location)



Social contacts and infection – conclusions

- Important to understand the mechanism of transmission through social contacts
- But studies to elucidate role are difficult
 - community-based, not clinical
 - few infections
 - prior immunity
- Role of contacts in driving transmission is subtle
- Location and community-scale information more helpful than individual-level information
- Warning to modellers
 - our understanding is incomplete



Derek Cummings
 Shanta Zimmer
 Chuck Vukotich
 SMART Study field team
 Amra Uzicanin & Jeanette Rainey (CDC)

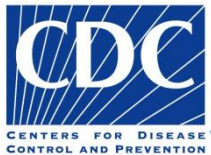
FLUSCAPE 流感景观

Immunological Landscapes of Influenza in China 在中国的流感免疫景观



Hong Kong Pandemic Flu study

On Kwok, Ben Cowling, Stephen Riley, Vivian Wei, Kendra Wu, Malik Perids (HKU)



广州市第十二人民医院
 Guangzhou Hospital No.12

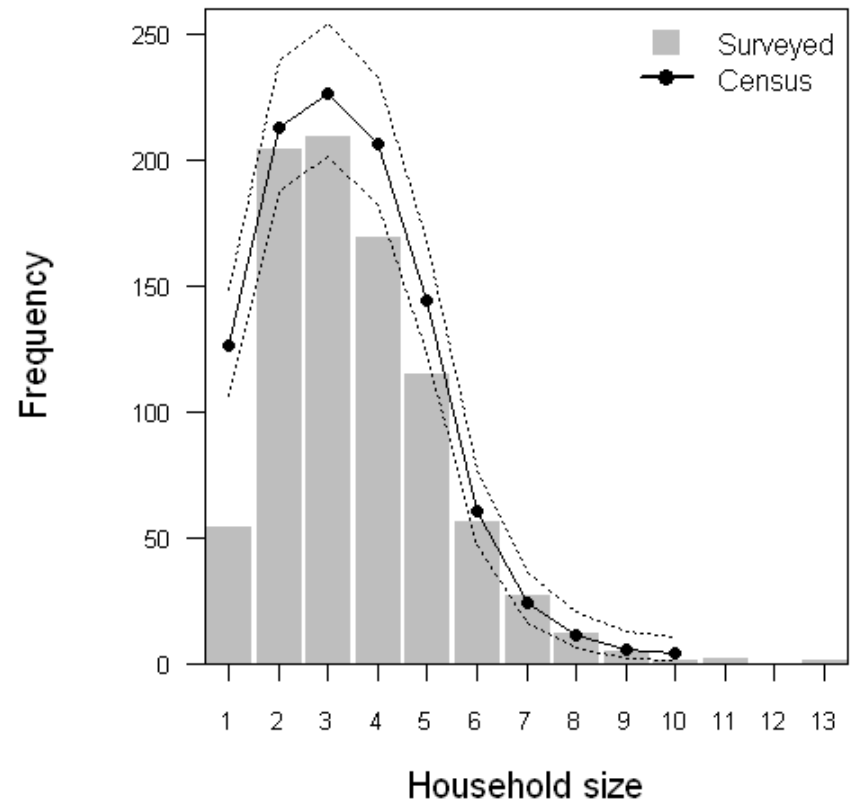
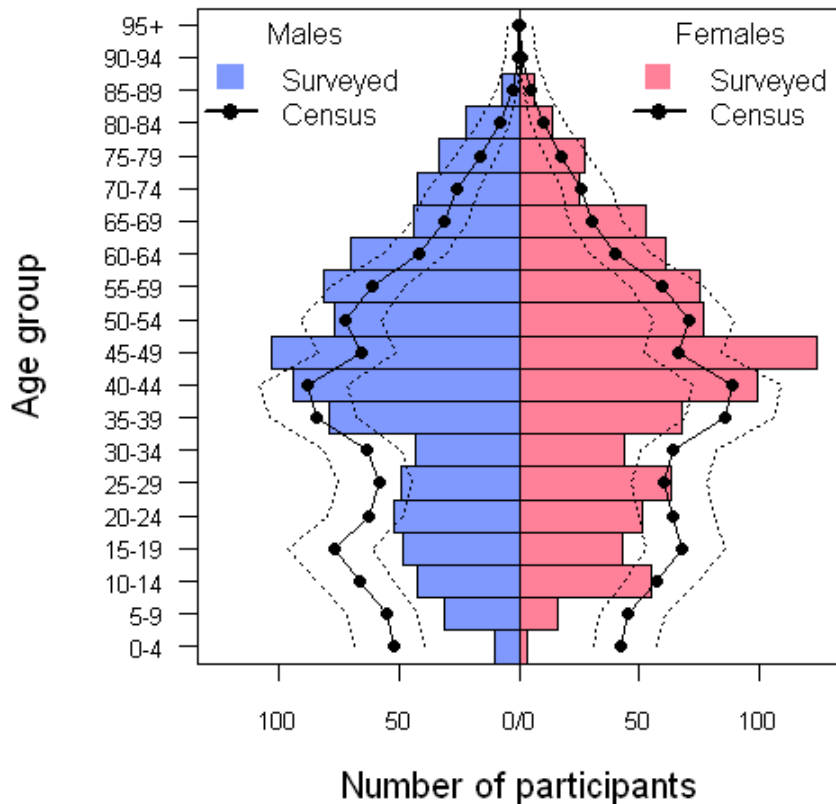


Imperial College
 London

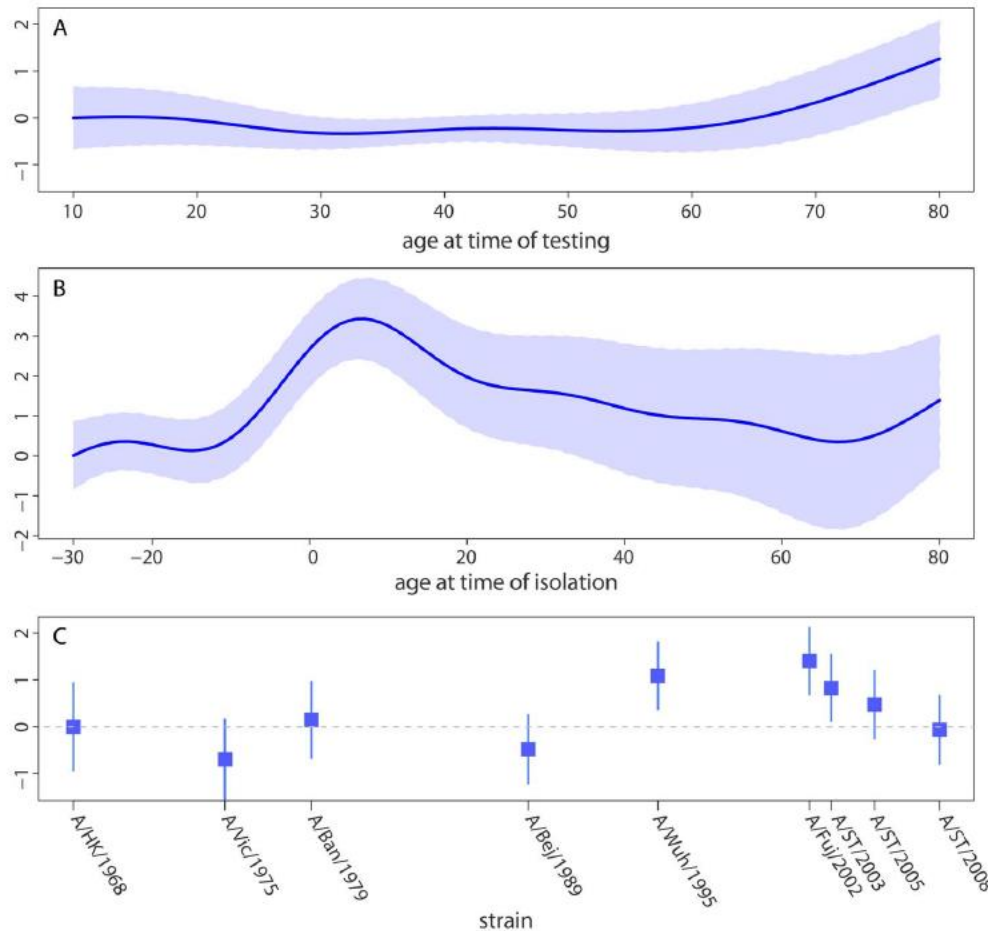
Additional slides

Study population

Participants = 1,838
 Households = 1,019
 Locations = 40



Antigenic seniority



- GAM regression modelling
- Those aged 5-10 at time of first circulation have highest titre
- Systematic decline with later strains
- Uptick?

Serology – summary

- Found significant age and location effects
- Strain-specific effects
- Antigenic Seniority – advances OAS
- What mechanisms generate observed differences in titre as such small spatial scales?
- Does social connectivity vary between study sites?

Figure S2. (A) Distributions of number of contacts split by density of household location. **(B)** Age distribution of participants split by density of household location. Density categories follow those described in the Methods section.

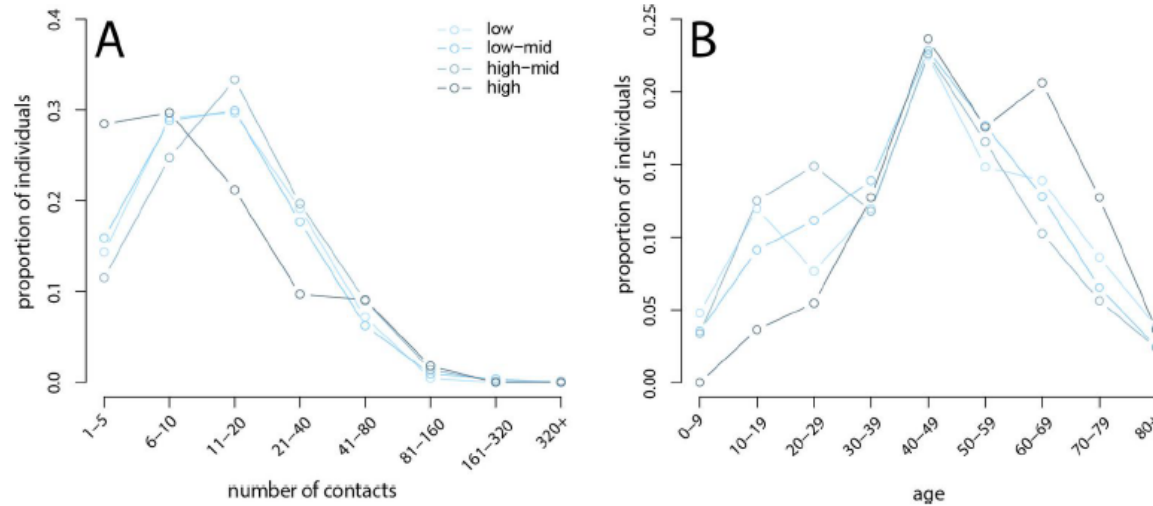


Figure S3. Distance kernels split by population density of participants' home location on (A) linear and (B) log scales. Density categories follow those described in the Methods section.

