

# Household clustering suggests a novel chemoprophylaxis trial design for an arboviral disease

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## Background

- Outbreaks of chikungunya and other Aedes mosquito-borne viral infections result in a huge burden of disease in tropical / subtropical regions
- Chikungunya virus (CHIKV) infection leads to acute febrile illness, disabling inflammation and pain in the joints
- Acute fever resolves in days, but musculoskeletal symptoms can persist for months and years
- Both treatment and prophylaxis against CHIKV infection are needed
- No randomised trials reported for treatment or chemoprophylaxis of acute CHIKV infection

## The problem

- Why have no chemoprophylaxis trials been reported?
- Outbreaks of chikungunya are challenging for studying interventions due to typical outbreak disease characteristics:
  - Unpredictability in time and place
  - Urgency due to rapid spread and short outbreak duration
  - Unknowns around disease course and pathophysiology
- High risk of outbreak ending before a trial can be concluded

## Potential solution

- Enrolling a high-risk population could permit a more feasible, smaller, shorter and conclusive trial
- Can we clearly identify a high-risk population?
- Within-household transmission of viral diseases as a target for antiviral prophylaxis
  - Precedents exist amongst respiratory viruses
  - Successful prevention of secondary household infections by influenza and SARS-CoV-2 viruses
- Could this be a viable model for testing intervention against a mosquito-borne virus?

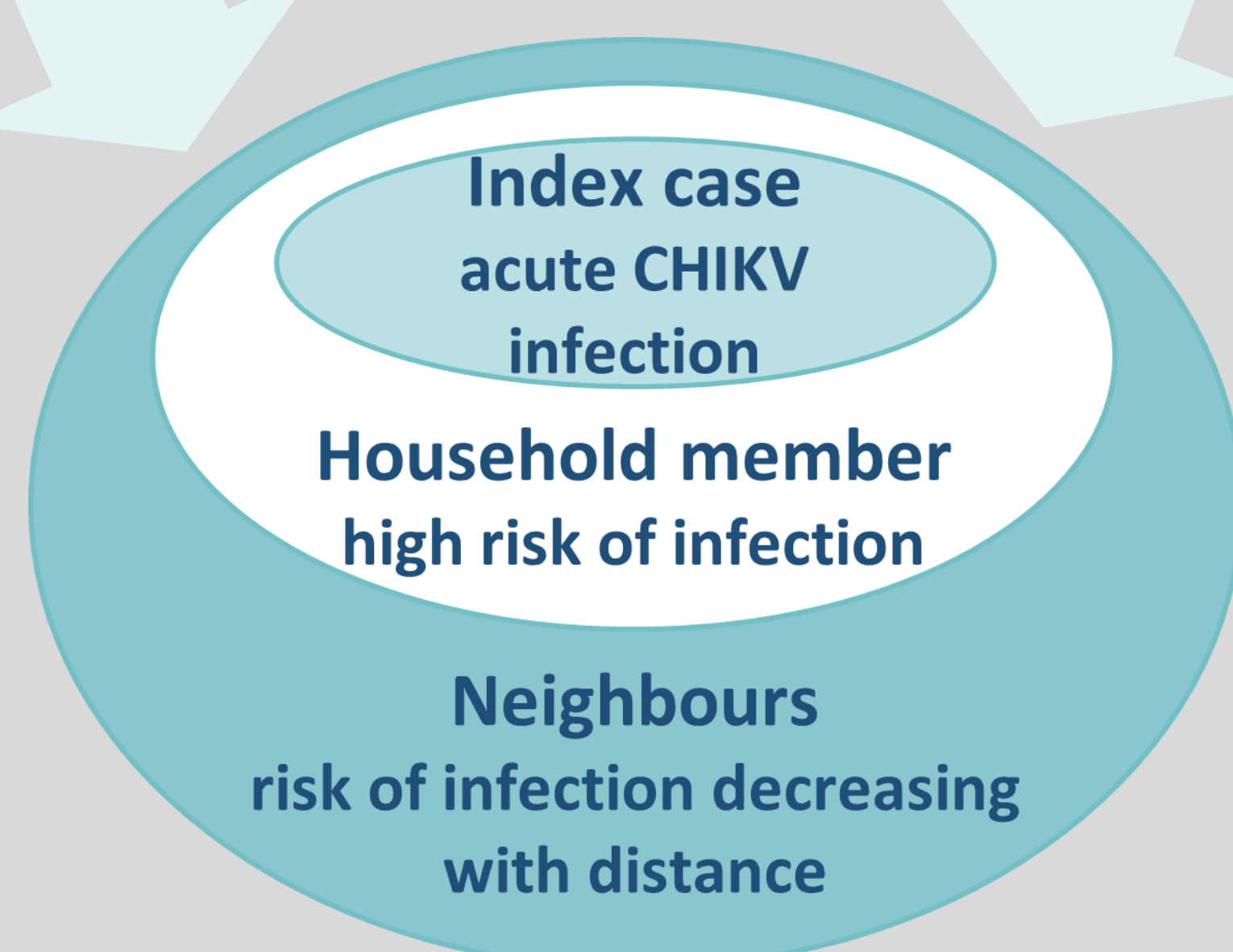
## Current evidence supports increased risk of secondary household infections in chikungunya outbreaks

Spatial microclustering of CHIKV cases in Puerto Rico  
**30% estimate**  
of 2° infection risk <50m<sup>1</sup>

Clustering of cases along one street, Salvador, Brazil<sup>2</sup>

Household clustering of CHIKV cases in Bangladesh<sup>3</sup>, South India<sup>4</sup>, Dominica<sup>5</sup>  
**12%-26%**  
estimates of household 2° infection risk

Household clustering of other Aedes-transmitted viruses:  
**20%-30%** household 2° infection risk of Dengue in Thailand<sup>10-13</sup>, Zika clustering in Martinique<sup>14</sup>



## Limited range of Aedes mosquito from release-recapture studies in:

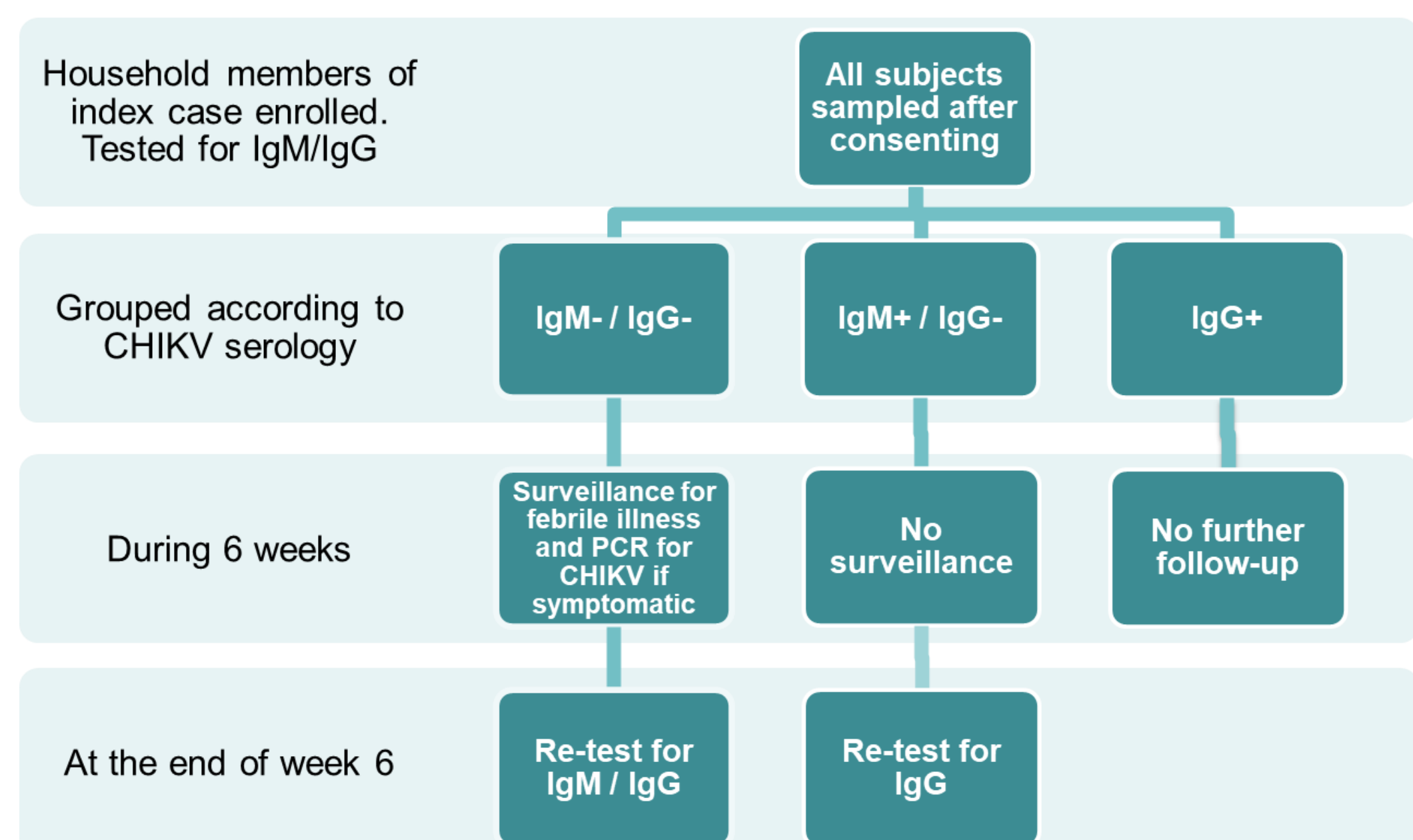
Puerto Rico<sup>6</sup>  
Hawaii<sup>7</sup>  
Thailand<sup>6</sup>  
La Reunion<sup>8</sup>  
Peru<sup>9</sup>



## Next step: Prospective surveillance of household contacts

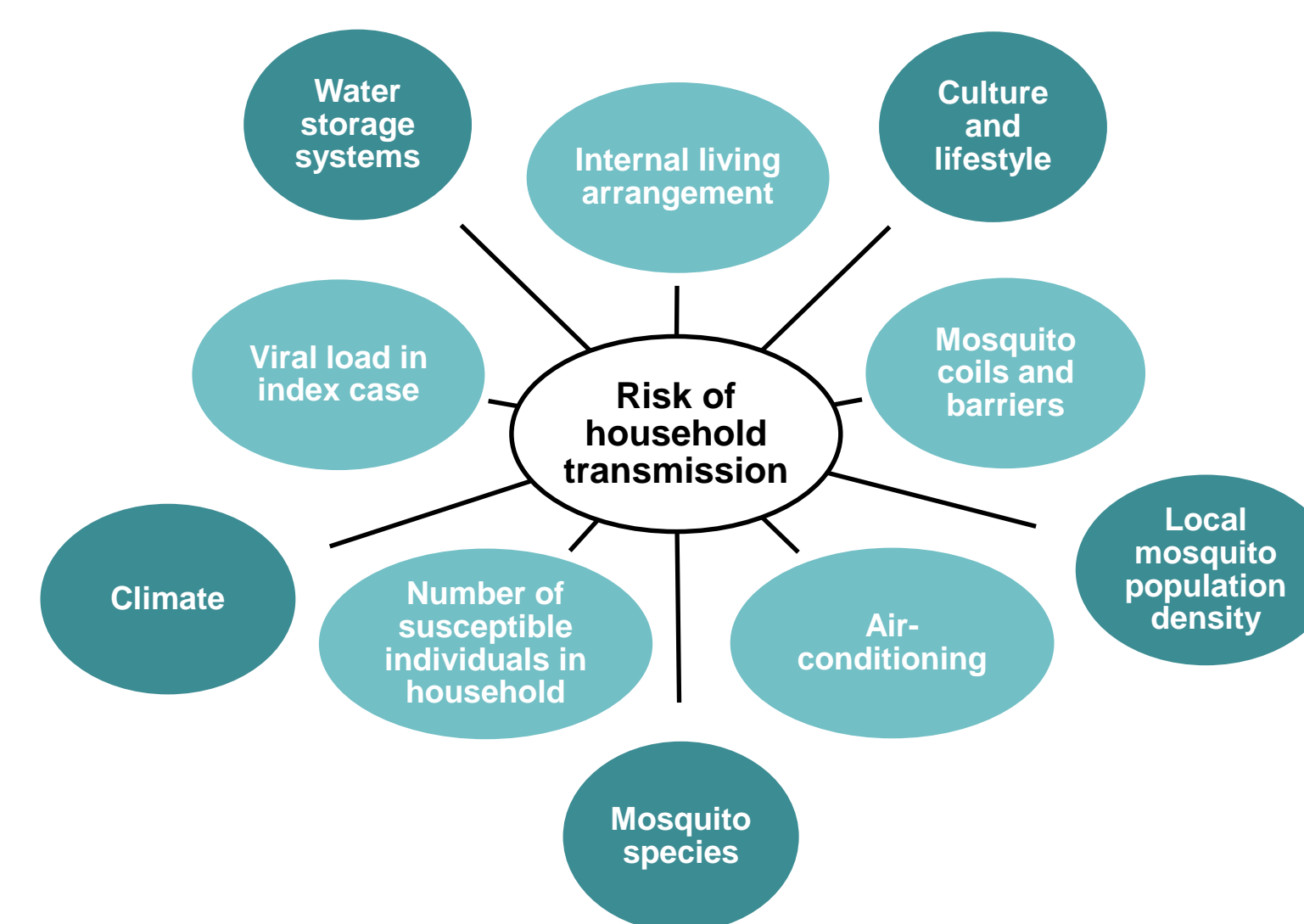
Surveillance study design to determine household secondary attack rate

- Index cases identified by RT-PCR confirmation of CHIKV infection



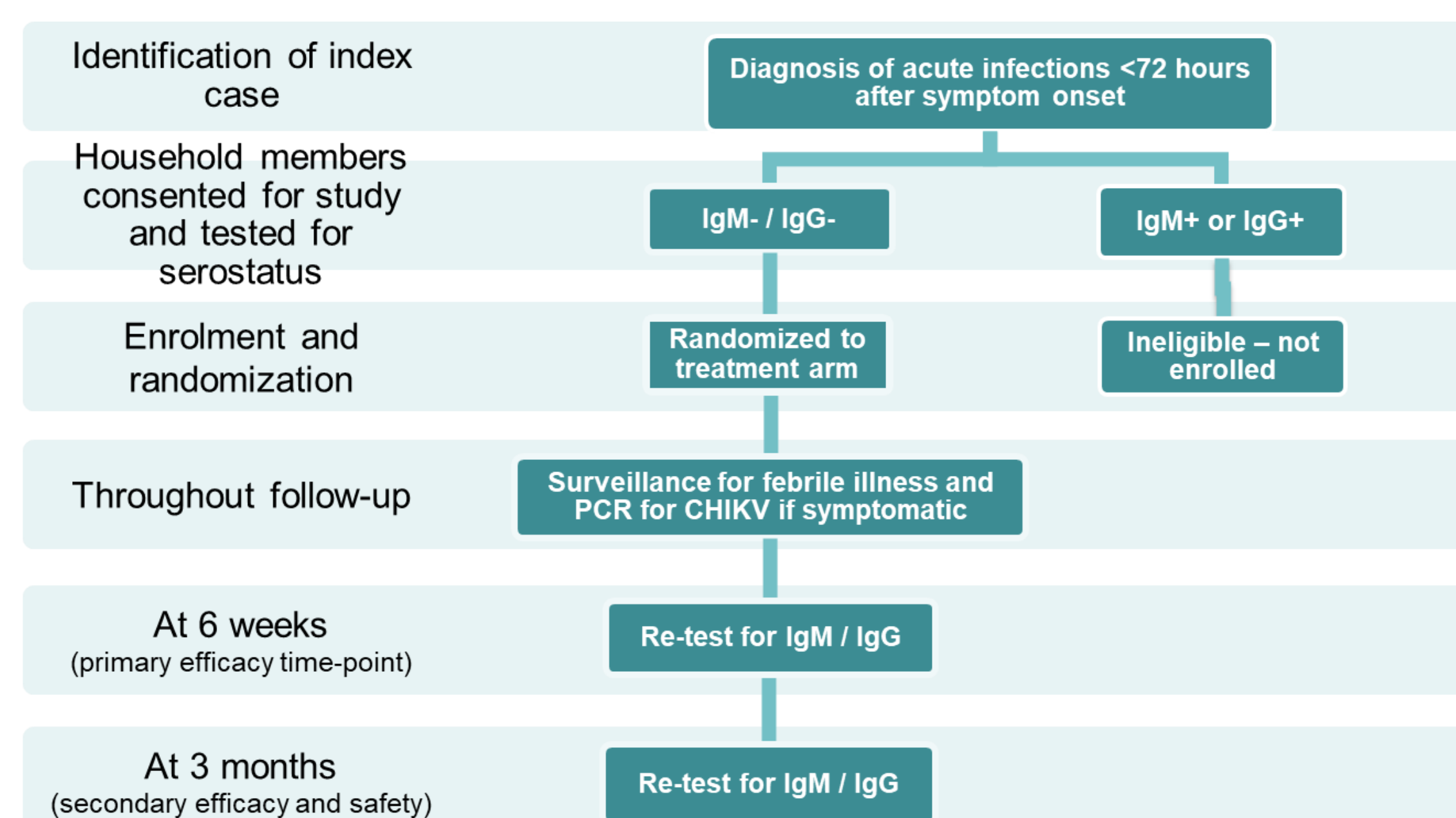
## Influences on the secondary attack rate

- Local factors contributing to infection risk for an index case
- Additional factors potentially contributing to the secondary attack rate within households



## Final step: a trial to demonstrate chemoprophylaxis efficacy

A future chemoprophylaxis trial could be based on the estimated rate of secondary household infections



## Issues and Perspectives

- Household secondary attack rates may not be accurately predicted from one chikungunya outbreak to another
- Estimates of household secondary attack rates from different countries and cultural environments are needed
- The objective is to have a range of estimates around which
  - Feasibility of prophylaxis trials could be evaluated
  - Sample size can be calculated
  - Evidence-based prophylaxis trials can be conducted

## References

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