Individually Randomized Clinical Trials

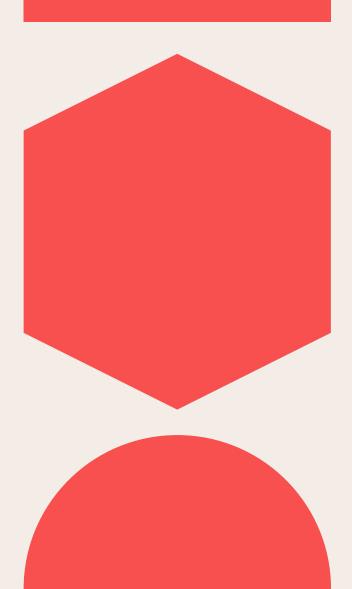
For Generating high-quality evidence on existing vaccines for Chikungunya in response to outbreaks

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Pros and Cons of Individual Randomization

Pros:

- Seamlessly combine information from prospectively randomized cohorts and outbreak clusters / rings
- Allows stratification on 1-2 important individual factors
- Statistically Efficient
 - Likely to require a smaller sample size
 - Faster answer
- Automatically balances:
 - Individual risk factors
 - Factors that differ between clusters
 - "Super-spreaders"

Cons (Within Rings):

- Logistics may be harder than a cluster-randomized design
- If there is a substantial indirect effect, could result in few/no cases in many clusters
- Some people have questioned ethics / appropriateness of vaccinating some family members and not others
- Blinding may be more challenging as vaccine and control must match closely (but is still very important to prevent bias!!!)



Potential (Simplified) Design

Assume:

- 2% incidence in unvaccinated participants
- 70% Vaccine Efficacy (VE)
- 90% Power
- 0.05 Type 1 error rate; Two-sided test
- Goal is to rule out VE=0

Then:

- → Total Sample Size ~ 2,750
 - 55 rings of average size 50
 - o 110 rings of average size 25

