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Individually Randomized Clinical Trials

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

Martha Nason

mnason@path.org

Director, Statistics and Data Management

Center for Vaccine Innovation and Access (CVIA)

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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!!!)*

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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
  - 110 rings of average size 25