World Health Organization

Chikungunya: possible study designs

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Powering research to prevent epidemics

Consider trial design in the context of information we need

We have two approved vaccines, but both are conditional (or accelerated in the US)

Data to support approval was based on antibody responses– neutralizing antibodies or passively transferred antibodies from vaccinees that showed protection in NHPs

Additional confirmatory data are desired for both

Neither are yet prequalified

We don’t yet know the best way to use these vaccines

Additional safety data is always useful, but need to be careful not to confound disease effects with vaccine effects

Some practical considerations

Likelihood and impact of previous immunity in the population

Time to develop immune response

Vaccine supply

Study goals

Trial design options

- Real time vs population-based risk assessment
  - Real-time risk assessment, e.g., ring vaccination
  - Population based risk assessment, e.g., HCWs
- Randomized trials
  - Individually randomized
    - Placebo or active controlled RCTs
    - Immediate vs delayed vaccination
    - Randomization during deployment
  - Cluster randomized
    - Define clusters geographically (e.g. mosquito range-based)
    - Step wedge is almost never appropriate for epidemic settings

Considerations for real-world data

Pragmatic trials

Non-randomized studies strategies to address potential bias

- Need to address potential confounders (e.g., mosquito spraying, nets, other risk factors, etc.)
- Consider potential case ascertainment biases
- Consider additional potential sources of bias inherent to observational studies
- Collect sufficient additional endpoints to assess potential bias
  - E.g., falsification outcomes
- Evaluate study for internal consistency
- Prospectively written protocol with prespecified endpoints and analysis methods
- More than one study showing similar results
- Note that large differences between groups may overcome some of the concerns regarding observational studies