

# Analysis of Cluster Randomized Test-Negative Designs: Cluster-Level Methods

## Supplementary Materials

| Cluster ID | Distribution of Dengue Cases | Distribution of OFI Controls |
|------------|------------------------------|------------------------------|
| 1          | 52                           | 138                          |
| 2          | 74                           | 212                          |
| 3          | 54                           | 125                          |
| 4          | 72                           | 145                          |
| 5          | 46                           | 165                          |
| 6          | 42                           | 194                          |
| 7          | 70                           | 250                          |
| 8          | 50                           | 131                          |
| 9          | 73                           | 229                          |
| 10         | 69                           | 156                          |
| Total      | 602                          | 1745                         |

Table 1: Hypothetical dengue and other febrile illness (OFI) count data for an example of 10 clusters used for permutation distribution estimates.

| Cluster ID | Period    |           |           |           |           |           |           |           |           |
|------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|            | '03 - '05 | '05 - '06 | '06 - '07 | '07 - '08 | '08 - '10 | '10 - '11 | '11 - '12 | '12 - '13 | '13 - '14 |
| 1          | 13        | 19        | 37        | 29        | 42        | 48        | 18        | 26        | 34        |
| 2          | 14        | 14        | 30        | 27        | 34        | 37        | 15        | 25        | 34        |
| 3          | 35        | 32        | 39        | 43        | 62        | 52        | 25        | 40        | 38        |
| 4          | 9         | 13        | 13        | 8         | 18        | 18        | 6         | 7         | 9         |
| 5          | 17        | 25        | 69        | 60        | 36        | 53        | 34        | 47        | 71        |
| 6          | 37        | 38        | 77        | 72        | 75        | 89        | 84        | 120       | 104       |
| 7          | 23        | 28        | 48        | 51        | 85        | 76        | 28        | 40        | 36        |
| 8          | 20        | 32        | 51        | 57        | 66        | 41        | 13        | 36        | 37        |
| 9          | 25        | 29        | 46        | 41        | 57        | 48        | 15        | 27        | 25        |
| 10         | 14        | 25        | 53        | 49        | 41        | 31        | 9         | 35        | 42        |
| 11         | 40        | 61        | 78        | 64        | 84        | 98        | 57        | 62        | 71        |
| 12         | 33        | 54        | 74        | 59        | 80        | 80        | 44        | 63        | 69        |
| 13         | 35        | 52        | 79        | 86        | 119       | 112       | 49        | 56        | 76        |
| 14         | 28        | 39        | 57        | 48        | 59        | 56        | 29        | 49        | 62        |
| 15         | 30        | 39        | 56        | 46        | 52        | 40        | 20        | 25        | 27        |
| 16         | 22        | 51        | 68        | 47        | 56        | 43        | 19        | 36        | 38        |
| 17         | 12        | 18        | 25        | 22        | 20        | 14        | 8         | 17        | 16        |
| 18         | 41        | 55        | 112       | 93        | 130       | 151       | 81        | 139       | 128       |
| 19         | 16        | 27        | 69        | 71        | 53        | 44        | 24        | 47        | 69        |
| 20         | 19        | 37        | 43        | 28        | 45        | 41        | 30        | 79        | 77        |
| 21         | 24        | 45        | 63        | 49        | 59        | 62        | 42        | 73        | 68        |
| 22         | 33        | 57        | 72        | 59        | 84        | 73        | 35        | 66        | 62        |
| 23         | 12        | 19        | 29        | 29        | 36        | 29        | 14        | 34        | 32        |
| 24         | 21        | 40        | 67        | 90        | 151       | 106       | 27        | 72        | 76        |

Table 2: *Dengue Case Counts*. The frequency of recorded (hospitalized) dengue fever cases in each of these 24 clusters for each of nine distinct two-year periods covering the time interval from 2003-2014. During this period, there was no available data for 2004 and 2009, so that the first two-year interval was for 2003 and 2005; similarly the 2008-10 interval included data for 2008 and 2010. Otherwise each two-year period covered consecutive years.

| Cluster ID | '14 – '15 |
|------------|-----------|
| 1          | 486       |
| 2          | 155       |
| 3          | 1197      |
| 4          | 255       |
| 5          | 249       |
| 6          | 710       |
| 7          | 658       |
| 8          | 714       |
| 9          | 478       |
| 10         | 376       |
| 11         | 388       |
| 12         | 426       |
| 13         | 842       |
| 14         | 547       |
| 15         | 285       |
| 16         | 586       |
| 17         | 344       |
| 18         | 484       |
| 19         | 151       |
| 20         | 223       |
| 21         | 522       |
| 22         | 804       |
| 23         | 286       |
| 24         | 792       |

Table 3: *OFI Counts*. Data for the distribution for OFIs is only available for one two-year period from 2014-15.

| Relative Risk ( $\lambda$ ) | Test-Positive Fraction | Odds Ratio | GEE    | Random Effects |
|-----------------------------|------------------------|------------|--------|----------------|
| 1                           | 0.0506                 | 0.0749     | 0.0000 | 0.0742         |
| 0.6                         | 0.5258                 | 0.5795     | 0.0014 | 0.6222         |
| 0.5                         | 0.7798                 | 0.8238     | 0.0103 | 0.8508         |
| 0.4                         | 0.9418                 | 0.9620     | 0.0805 | 0.9693         |
| 0.3                         | 0.9965                 | 0.9985     | 0.4175 | 0.9990         |

Table 4: The proportion of simulations that returned significant results for each intervention effect of interest ( $\lambda$ ) as in Table 2 of the paper, but now with 10,000 random intervention allocations of 1,000 cases and 1,000 controls ( $r = 1$ ).

| Relative Risk ( $\lambda$ ) | Test-Positive Fraction | Odds Ratio | GEE    | Random Effects |
|-----------------------------|------------------------|------------|--------|----------------|
| 1                           | 0.0013                 | 0.0104     | 0.0000 | 0.0043         |
| 0.6                         | 0.4783                 | 0.6055     | 0.0000 | 0.6462         |
| 0.5                         | 0.8075                 | 0.8864     | 0.0007 | 0.9166         |
| 0.4                         | 0.9732                 | 0.9852     | 0.0241 | 0.9919         |
| 0.3                         | 1.0000                 | 0.9998     | 0.3462 | 1.0000         |

Table 5: The proportion of simulations that returned significant results for each intervention effect of interest ( $\lambda$ ) as in Table 2 of the paper, but now with each approach applied to the results of the 494 constrained intervention allocations with 1,000 cases and 4,000 controls ( $r = 4$ ).

| Relative Risk ( $\lambda$ ) | Test-Positive Fraction | Odds Ratio | GEE    | Random Effects |
|-----------------------------|------------------------|------------|--------|----------------|
| 1                           | 0.0022                 | 0.0104     | 0.0000 | 0.0047         |
| 0.6                         | 0.5283                 | 0.6055     | 0.0000 | 0.6581         |
| 0.5                         | 0.8488                 | 0.8864     | 0.0007 | 0.9199         |
| 0.4                         | 0.9800                 | 0.9852     | 0.0241 | 0.9924         |
| 0.3                         | 1.0000                 | 0.9998     | 0.3462 | 1.0000         |

Table 6: The proportion of simulations that returned significant results for each intervention effect of interest ( $\lambda$ ) as in Supplementary Table 4, but now using the 494 constrained intervention allocations with 1,000 cases and 1,000 controls ( $r = 1$ )