## Supplementary information for:

# Cross-serotype interactions and disease outcome prediction of dengue infections in Vietnam

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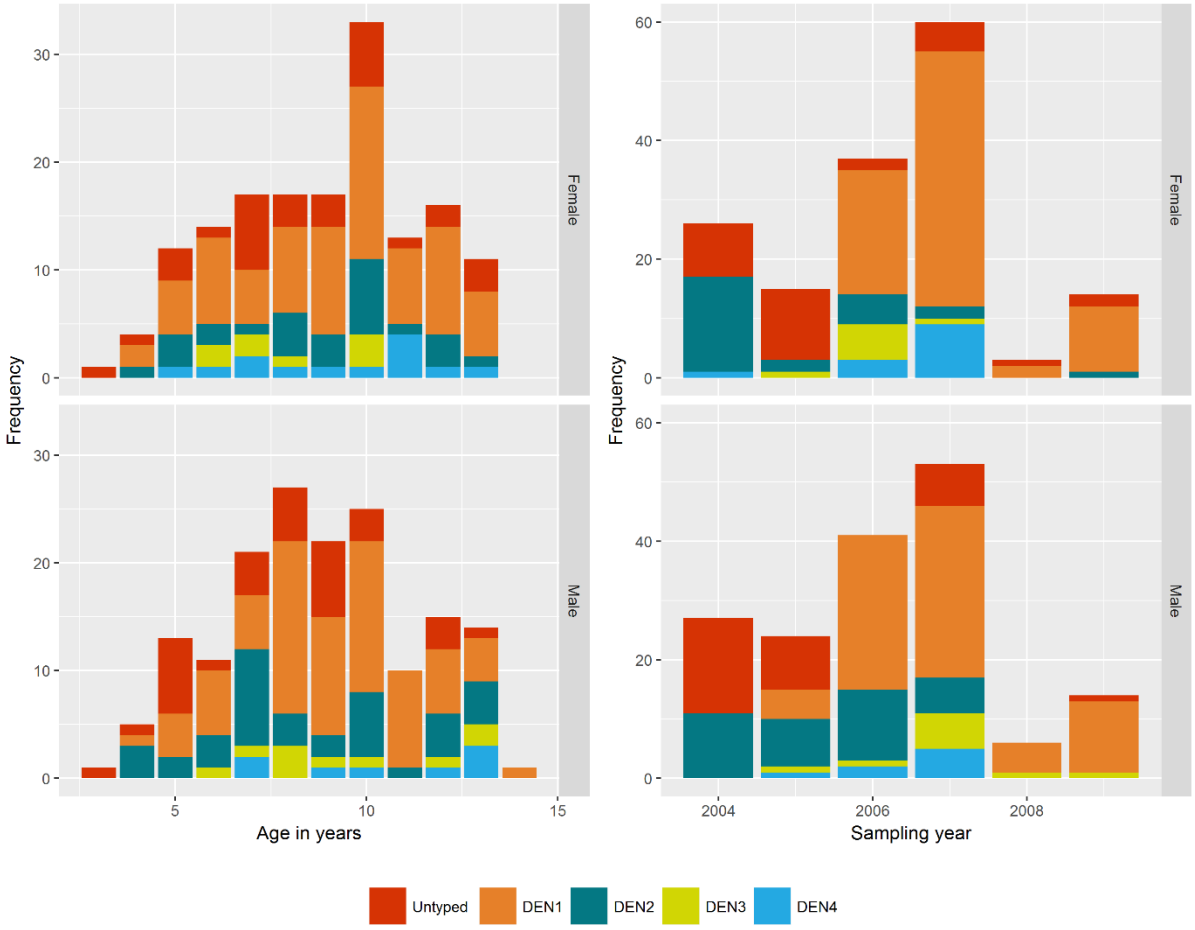
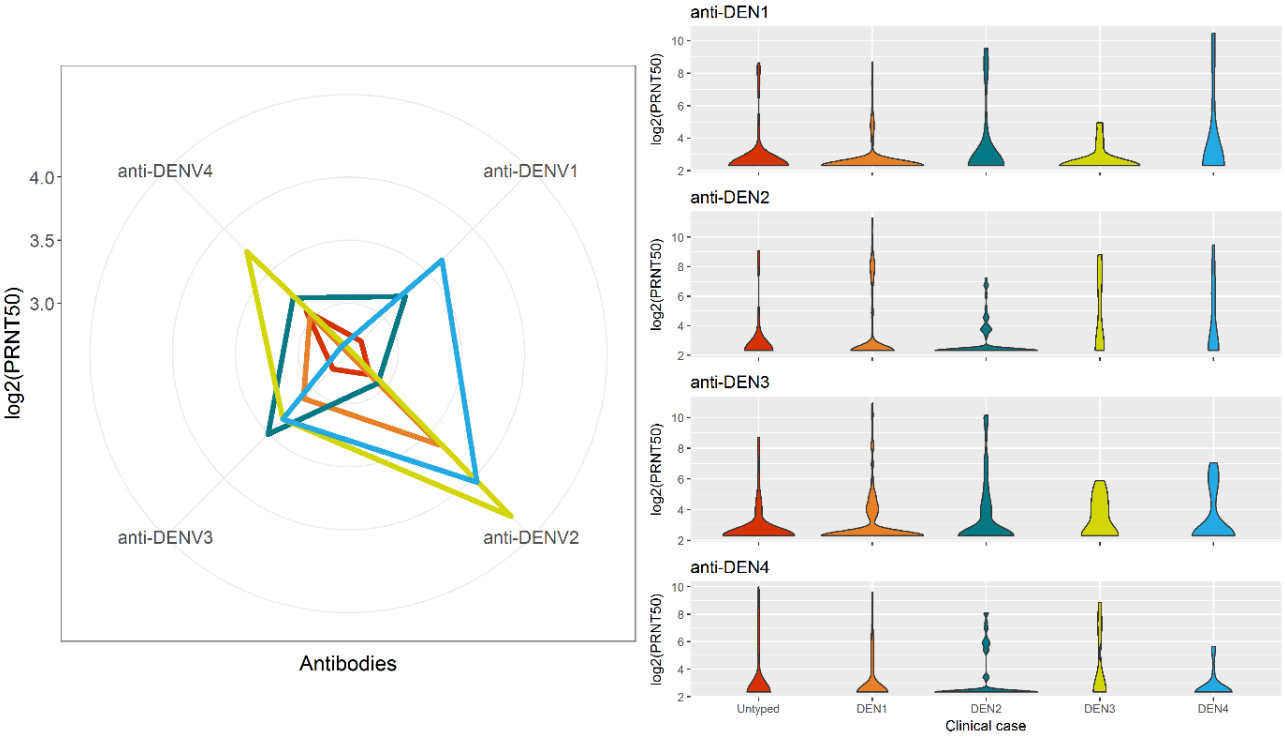
**Supplementary Figure S1. Epidemiological data collected over the study period. The panels on the left show the age profiles of dengue case occurrences during the study period by gender and serotype. The right most panels display clinical dengue illness time series by gender and serotype.**

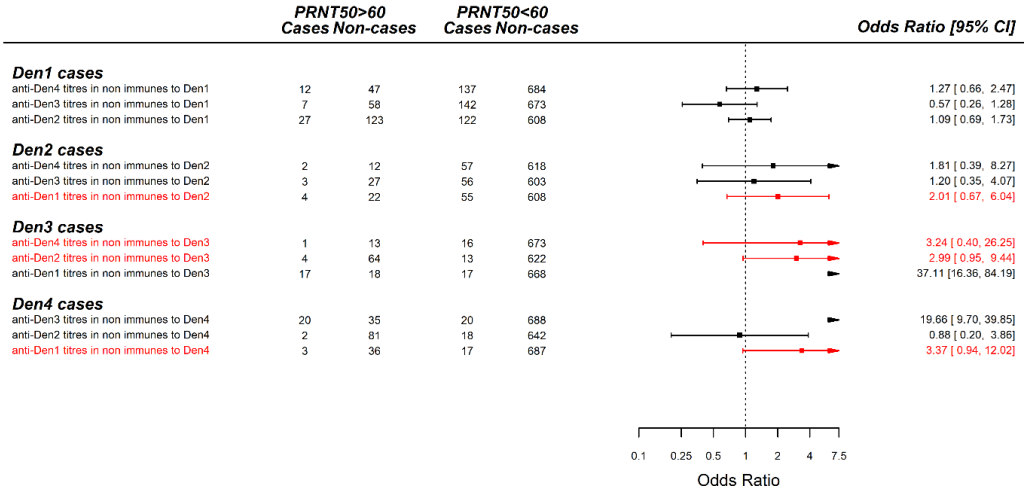


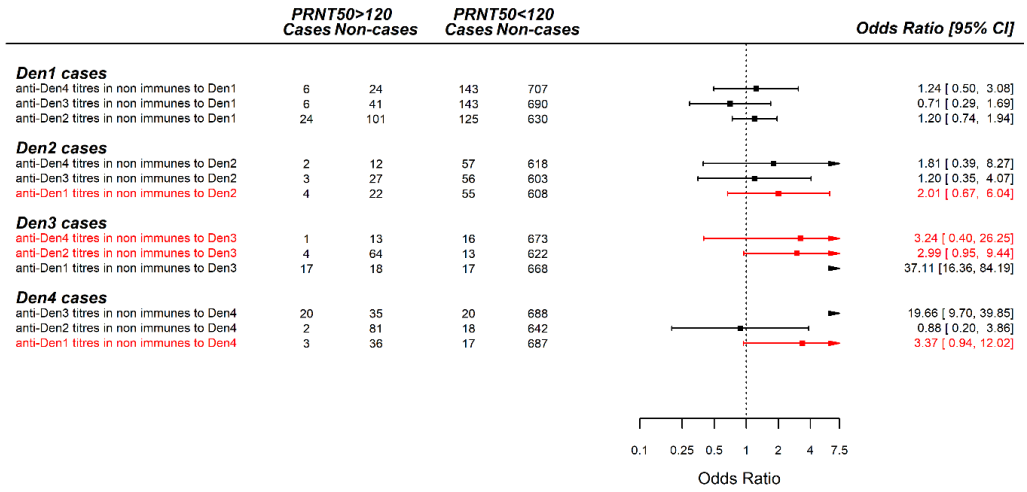
**Supplementary Figure S2. Measured antibody profiles of dengue cases. The radar plot on the left shows the mean anti-DENV titres measured in children with dengue fever. Each line is coloured according to the infecting dengue serotype. The violin plots on the right show the distribution of anti-DENV antibodies in clinical cases for each infecting serotype. Each panel refers to the measured PRNT50 titres against a specific serotype.**

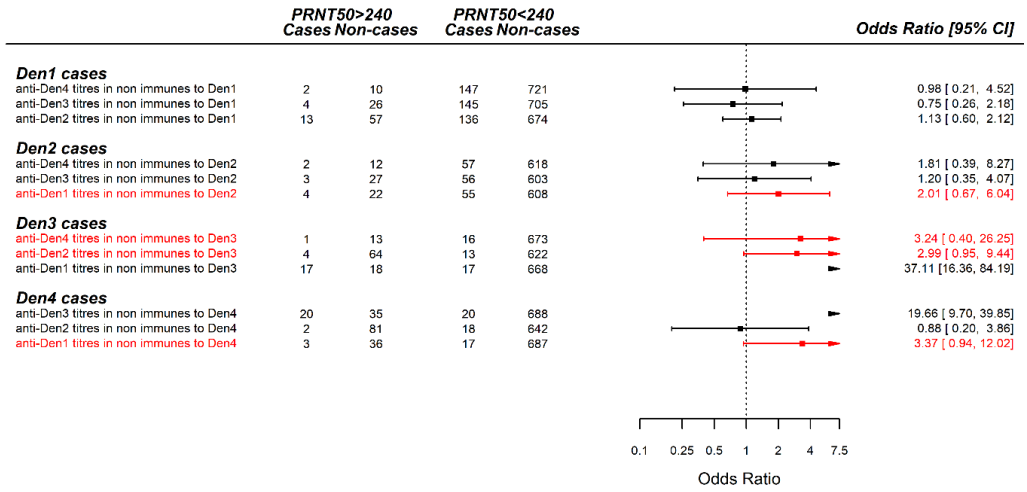


**Supplementary Figure S3. Odds ratio of dengue illness in the year following neutralising antibody titre measurements in children with different antibody repertoires. The top row of plots refers to children with monotypic immunity, i.e., only one antibody over PRNT50=40, while the bottom row is for children with at least two PRNT titres over 40.**

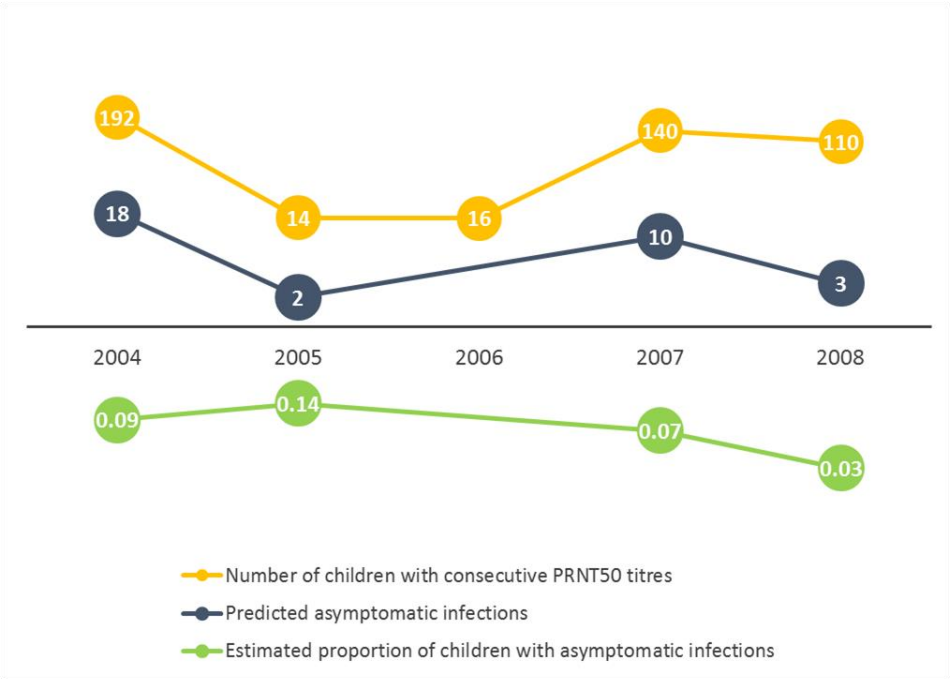
**Supplementary Figure S4. The odds ratio presented here refers to children with a homologous PRNT50 titre under 40, i.e., non-immune to the reference dengue serotype thus reflecting the ratio between the odds of having clinical dengue illness when immune to heterologous serotypes (conditional on having a PRNT50<40 to the homologous serotype) and the odds of becoming ill in the absence of immunity to any serotype.**

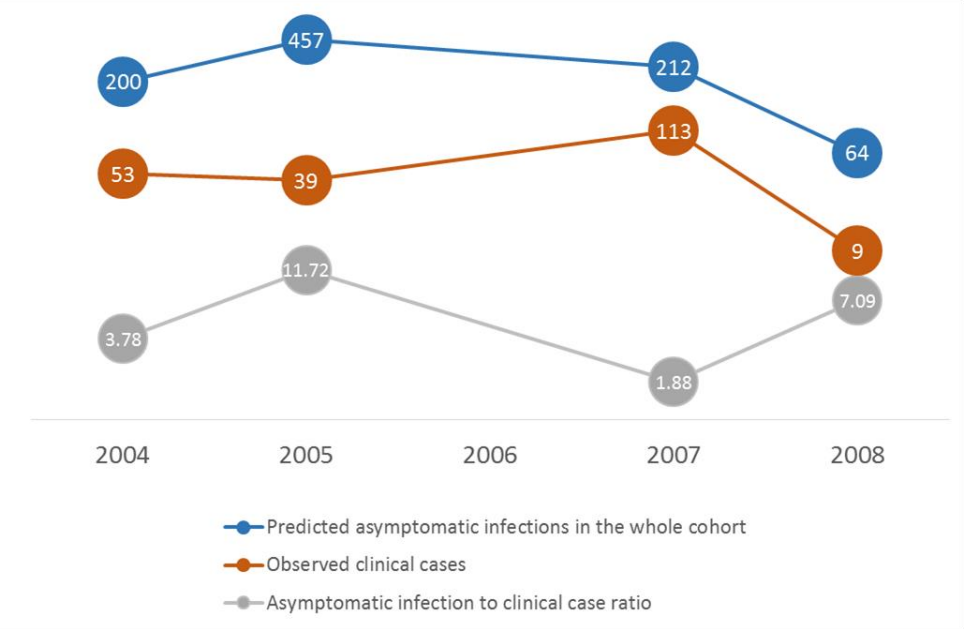


**Supplementary Figure S5. Predicted asymptomatic infections in the study cohort and estimated asymptomatic infection to clinical case ratios throughout the years. The yearly figures are presented as stacked lines on a logarithmic scale to highlight the temporal dynamics. We could not predict asymptomatic infections in 2006 due to the low number of PRNT50 measurements in non-clinical individuals.**



**Supplementary Table S1. Odds ratio of clinical dengue illness depending on multiple immunity cut-offs. BIS stands for baseline immune status, as defined in each scenario.**

| **Immune defined as having any PRNT50 titre >=10** | | |
|---|---|---|
| | **Immune** | **Naive** |
| Cases | 117 | 203 |
| Non cases | 374 | 488 |
| BIS OR | 0.752 (0.577-0.979) | |
| p-value | **0.0346** | |

| **Immune defined as having any PRNT50 titre >= 40** | | |
|---|---|---|
| | **Immune** | **Naive** |
| Cases | 102 | 218 |
| Non cases | 343 | 519 |
| BIS OR | 0.708(0.540-0.929) | |
| p-value | **0.0128** | |

| **Immune defined as having any PRNT50 titre >= 80** | | |
|---|---|---|
| | **Immune** | **Naive** |
| Cases | 83 | 237 |
| Non cases | 304 | 558 |
| BIS OR | 0.643(0.483-0.856) | |
| p-value | **0.0025** | |

| **Immune defined as having any PRNT50 titre >= 160** | | |
|---|---|---|
| | **Immune** | **Naive** |
| Cases | 66 | 254 |
| Non cases | 254 | 608 |
| BIS OR | 0.622 (0.457-0.846) | |
| p-value | **0.0025** | |

**Supplementary Table S2. Variables used in the multinomial regression models.**

| Name | Variable description |
|---|---|
| Age | Age in years (continuous) |
| Gender | Male or Female (binary) |
| $X_i$ | PRNT50 titres for each serotype (Log2 dilutions) |
| Year | Calendar year |
| BIS | Baseline immune status (any PRNT50 value over detectability limit = 1, else = 0) |
| BIS80 | Baseline immune status (any PRNT50 value over 80 =1, else = 0) |
| Multi | Multitypic baseline immune profile (over detection threshold for more than one serotype =1, else =0 ) |
| Multi40 | Multitypic baseline immune profile (PRNT50>40 for more than one serotype =1, else =0 |
| Multi80 | Multitypic baseline immune profile (PRNT50>80 for more than one serotype =1, else =0 |
| Skewedness | Skewedness of the concatenated vector of PRNT50 titres for all serotypes. Indicates the breadth (or lack thereof) of the antibody repertoire. |
| Dominance | Immune dominance indicator (if there is one PRNT50 value greater than twice the sum of all others =1, else 0) |
| $P_i$ | Immune status against each serotype (binary – 1 if over detection limit, 0 otherwise) |
| $P80_i$ | Immune status against each serotype (binary – 1 if PRNT50>80, 0 otherwise) |
| IgG | IGG titre measured by an ELISA test |
| IgM | IGM titre measured by an ELISA test |
| IgGp | Positive IGG test (binary- 1 if GOD/cut-off>1.1, 0 otherwise) |
| IgMp | Positive IGM test (binary- 1 if GOD/cut-off>1.1, 0 otherwise) |

**Supplementary Table S3. Multinomial logistic regression models explored.**

| Variable | Model | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 |
| Age | | | x | x | | | x | | | | | | x | x | | | | | | | | | |
| Gender | | x | | x | | | x | | | | | | | | | | | | | | | | |
| $X_i$ | x | x | x | x | x | x | x | x | | | | | | | | x | x | x | | x | | | |
| Year | | | | | | | | | | | | | | | | | | | | | | | |
| BIS | | | | | x | | | | x | x | | | | x | x | | | | | | | | |
| BIS80 | | | | | | x | x | | | | x | x | x | | | | | | | | x | | |
| Multi | | | | | | | | x | | x | | x | x | x | | | | | | | | x | x |
| Multi40 | | | | | | | | | | | | | | | | | x | | | | | | |
| Multi80 | | | | | | | | | | | | | | | | | | x | | | | | |
| Skewedness | | | | | | | | | | | | | | | | | | | | | | x | |
| Dominance | | | | | | | | | | | | | | | x | x | | | | | x | | |
| $P_i$ | | | | | | | | | | | | | | | | | | | x | x | | | x |
| $P80_i$ | | | | | | | | | | | | | | | | | | | | | | | |
| IGG | | | | | | | | | | | | | | | | | | | | | | | |
| IGM | | | | | | | | | | | | | | | | | | | | | | | |
| IGGp | | | | | | | | | | | | | | | | | | | | | | | |
| IGMp | | | | | | | | | | | | | | | | | | | | | | | |

| Variable | Model | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 | 41 | 42 | 43 | 44 | 45 | 46 |
| Age | | | | x | | | x | | | | | | | | | | | x | | | x | | x |
| Gender | | | | | x | | | | | | | | | | | | | | | | | | x |
| $X_i$ | | | x | x | x | x | x | | | | | | | | x | x | x | x | x | x | x | x | |
| Year | | | | | | | | | | | | | | | | | | | | | | | |
| BIS | | | | | | | x | | | | | | | | | | | | | | | | |
| BIS80 | | | | | | | | | | | | | | | | | | | | | | | |
| Multi | | | | x | x | | | | | | | | | | | | | | | | | | |
| Multi40 | x | | x | | | x | | x | | | | | | | | | x | x | x | x | x | | |
| Multi80 | | | | | | | | | x | | | | | | | | | | | | | | |
| Skewedness | | | | | | x | | | | | | | | | | | | | | | | | |
| Dominance | | | x | | | | | | | | | | | | | | | | x | | | | |
| $P_i$ | x | | | | | | | | | | | | | | | | | | | | | | |
| $P80_i$ | | x | | | | | | | | | | | | | | | | | | | | | |
| IGG | | | | | | | | | | x | | | | x | x | | x | x | x | x | x | x | |
| IGM | | | | | | | | | | | x | | | x | x | | x | x | x | | | | |
| IGGp | | | | | | | | | | | | x | | | | x | | | | | | | |
| IGMp | | | | | | | | | | | | | x | | | x | | | | | | | |

| Variable | Model | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 47 | 48 | 49 | 50 | 51 | 52 | 53 | 54 | 55 | 56 | 57 | 58 | 59 | 60 | 61 | 62 | 63 | 64 | 65 | 66 | 67 | 68 | 69 |
| Age | | | x | x | | | x | | | | | | x | x | | | | | | | | | |
| Gender | | x | | x | | | x | | | | | | | | | | | | | | | | |
| $X_i$ | x | x | x | x | x | x | x | x | | | | | | | | x | x | x | | x | | | |
| Year | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x |
| BIS | | | | | x | | | | x | x | | | | x | x | | | | | | | | |
| BIS80 | | | | | | x | x | | | | x | x | x | | | | | | | | x | | |
| Multi | | | | | | | | x | | x | | x | x | x | | | | | | | | x | x |
| Multi40 | | | | | | | | | | | | | | | | | x | | | | | | |
| Multi80 | | | | | | | | | | | | | | | | | | x | | | | | |
| Skewedness | | | | | | | | | | | | | | | | | | | | | | x | |
| Dominance | | | | | | | | | | | | | | | x | x | | | | | x | | |
| $P_i$ | | | | | | | | | | | | | | | | | | | x | x | | | x |
| $P80_i$ | | | | | | | | | | | | | | | | | | | | | | | |
| IGG | | | | | | | | | | | | | | | | | | | | | | | |
| IGM | | | | | | | | | | | | | | | | | | | | | | | |
| IGGp | | | | | | | | | | | | | | | | | | | | | | | |

| IGMp | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Variable** | **Model** | | | | | | | | | | | | | | | | | | | | | | |
| | 70 | 71 | 72 | 73 | 74 | 75 | 76 | 77 | 78 | 79 | 80 | 81 | 82 | 83 | 84 | 85 | 86 | 87 | 88 | 89 | 90 | 91 | 92 |
| Age | | | | x | | | x | | | | | | | | | | | x | | | x | | x |
| Gender | | | | | x | | | | | | | | | | | | | | | | | | x |
| $X_i$ | | | x | x | x | x | X | | | | | | | | x | x | x | x | x | x | x | x | |
| Year | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x |
| BIS | | | | | | | x | | | | | | | | | | | | | | | | |
| BIS80 | | | | | | | | | | | | | | | | | | | | | | | |
| Multi | | | | x | x | | | | | | | | | | | | | | | | | | |
| Multi40 | x | | x | | | x | | x | | | | | | | | | x | x | x | x | x | | |
| Multi80 | | | | | | | | | x | | | | | | | | | | | | | | |
| Skewedness | | | | | | x | | | | | | | | | | | | | | | | | |
| Dominance | | | x | | | | | | | | | | | | | | | | x | | | | |
| $P_i$ | x | | | | | | | | | | | | | | | | | | | | | | |
| $P80_i$ | | x | | | | | | | | | | | | | | | | | | | | | |
| IGG | | | | | | | | | | x | | | | x | x | | x | x | x | x | x | x | |
| IGM | | | | | | | | | | | x | | | x | x | | x | x | x | | | | |
| IGGp | | | | | | | | | | | | x | | | | x | | | | | | | |
| IGMp | | | | | | | | | | | | | x | | | x | | | | | | | |

**Supplementary Table S4. Model evaluation and selection. We underline models with AIC less than 4 AIC units away from the minimum AIC value.**

| Model | AIC | Number of parameters | AUC1 | AUC2 | AUC3 | AUC4 |
|---|---|---|---|---|---|---|
| **1** | 1706.5 | 20 | 0.590 | 0.623 | 0.694 | 0.644 |
| **2** | 1711.4 | 24 | 0.587 | 0.650 | 0.683 | 0.688 |
| **3** | 1708.9 | 24 | 0.613 | 0.618 | 0.677 | 0.697 |
| **4** | 1713.8 | 28 | 0.611 | 0.654 | 0.673 | 0.727 |
| **5** | 1711.7 | 24 | 0.587 | 0.650 | 0.683 | 0.688 |
| **6** | 1713.4 | 24 | 0.590 | 0.623 | 0.693 | 0.655 |
| **7** | 1713.4 | 24 | 0.590 | 0.623 | 0.693 | 0.655 |
| **8** | 1709.3 | 24 | 0.597 | 0.653 | 0.692 | 0.659 |
| **9** | 1750.5 | 8 | 0.528 | 0.515 | 0.538 | 0.502 |
| **10** | 1752.5 | 12 | 0.552 | 0.522 | 0.570 | 0.533 |
| **11** | 1746.1 | 8 | 0.541 | 0.536 | 0.555 | 0.502 |
| **12** | 1751.6 | 12 | 0.538 | 0.549 | 0.551 | 0.500 |
| **13** | 1753.6 | 16 | 0.565 | 0.559 | 0.566 | 0.603 |
| **14** | 1755.0 | 16 | 0.577 | 0.552 | 0.575 | 0.607 |
| **15** | 1753.9 | 12 | 0.533 | 0.516 | 0.588 | 0.563 |
| **16** | 1714.0 | 24 | 0.591 | 0.611 | 0.694 | 0.643 |
| **17** | 1707.1 | 24 | 0.595 | 0.625 | 0.690 | 0.643 |
| **18** | 1710.8 | 24 | 0.589 | 0.611 | 0.675 | 0.647 |
| **19** | 1742.3 | 20 | 0.597 | 0.566 | 0.597 | 0.615 |
| **20** | 1718.7 | 36 | 0.609 | 0.663 | 0.731 | 0.648 |
| **21** | 1748.1 | 12 | 0.549 | 0.541 | 0.576 | 0.555 |
| **22** | 1747.9 | 12 | 0.561 | 0.504 | 0.550 | 0.539 |
| **23** | 1751.6 | 12 | 0.531 | 0.510 | 0.578 | 0.569 |
| **24** | 1739.3 | 12 | 0.548 | 0.545 | 0.572 | 0.532 |
| **25** | 1710.3 | 20 | 0.576 | 0.606 | 0.704 | 0.604 |
| **26** | 1713.8 | 28 | 0.595 | 0.628 | 0.691 | 0.665 |
| **27** | 1711.1 | 28 | 0.617 | 0.670 | 0.677 | 0.706 |
| **28** | 1714.4 | 28 | 0.593 | 0.667 | 0.682 | 0.682 |
| **29** | 1712.7 | 28 | 0.592 | 0.626 | 0.674 | 0.633 |
| **30** | 1713.9 | 28 | 0.613 | 0.651 | 0.695 | 0.701 |
| **31** | 1733.5 | 8 | 0.551 | 0.544 | 0.510 | 0.522 |
| **32** | 1735.5 | 8 | 0.543 | 0.531 | 0.502 | 0.506 |
| **33** | 1747.3 | 8 | 0.551 | 0.589 | 0.666 | 0.661 |
| **34** | 1745.1 | 8 | 0.506 | 0.549 | 0.639 | 0.607 |
| **35** | 1747.0 | 8 | 0.530 | 0.540 | 0.543 | 0.522 |
| **36** | 1751.3 | 8 | 0.500 | 0.504 | 0.504 | 0.504 |
| **37** | 1750.0 | 12 | 0.513 | 0.582 | 0.641 | 0.623 |
| **38** | 1706.7 | 28 | 0.623 | 0.647 | 0.733 | 0.748 |
| **39** | 1715.4 | 28 | 0.605 | 0.638 | 0.709 | 0.662 |
| **40** | 1706.2 | 32 | 0.621 | 0.682 | 0.729 | 0.763 |
| **41** | 1707.4 | 36 | 0.624 | 0.669 | 0.734 | 0.772 |
| **42** | 1712.8 | 36 | 0.623 | 0.676 | 0.729 | 0.766 |
| **43** | 1704.6 | 28 | 0.620 | 0.684 | 0.744 | 0.768 |
| **44** | 1705.8 | 32 | 0.622 | 0.669 | 0.737 | 0.749 |
| **45** | 1704.6 | 24 | 0.623 | 0.647 | 0.749 | 0.742 |
| **46** | 1753.8 | 12 | 0.526 | 0.553 | 0.528 | 0.627 |
| ***47*** | ***1643.8*** | 24 | 0.702 | 0.755 | 0.749 | 0.672 |
| **48** | 1648.4 | 28 | 0.705 | 0.760 | 0.751 | 0.700 |
| ***49*** | ***1639.9*** | 28 | 0.711 | 0.765 | 0.741 | 0.691 |
| **50** | 1644.1 | 32 | 0.711 | 0.770 | 0.738 | 0.723 |
| **51** | 1649.9 | 28 | 0.705 | 0.760 | 0.751 | 0.700 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **52** | 1650.8 | 28 | 0.707 | 0.755 | 0.749 | 0.696 |
| **53** | 1650.8 | 28 | 0.707 | 0.755 | 0.749 | 0.696 |
| **54** | 1647.9 | 28 | 0.703 | 0.754 | 0.744 | 0.701 |
| **55** | 1693.5 | 12 | 0.661 | 0.712 | 0.578 | 0.546 |
| **56** | 1694.7 | 16 | 0.685 | 0.716 | 0.594 | 0.625 |
| **57** | 1689.4 | 12 | 0.668 | 0.706 | 0.580 | 0.553 |
| **58** | 1693.8 | 16 | 0.680 | 0.713 | 0.586 | 0.575 |
| **59** | 1688.0 | 20 | 0.670 | 0.728 | 0.608 | 0.612 |
| **60** | 1688.9 | 20 | 0.671 | 0.728 | 0.621 | 0.617 |
| **61** | 1695.9 | 16 | 0.666 | 0.712 | 0.612 | 0.625 |
| **62** | 1651.4 | 28 | 0.704 | 0.757 | 0.750 | 0.670 |
| **63** | 1646.2 | 28 | 0.705 | 0.755 | 0.747 | 0.711 |
| **64** | 1649.2 | 28 | 0.702 | 0.755 | 0.754 | 0.674 |
| **65** | 1683.9 | 24 | 0.701 | 0.715 | 0.650 | 0.665 |
| **66** | 1662.1 | 40 | 0.717 | 0.763 | 0.759 | 0.703 |
| **67** | 1691.2 | 16 | 0.677 | 0.712 | 0.601 | 0.618 |
| **68** | 1688.7 | 16 | 0.688 | 0.713 | 0.590 | 0.592 |
| **69** | 1692.2 | 16 | 0.674 | 0.713 | 0.608 | 0.612 |
| **70** | 1681.7 | 16 | 0.689 | 0.714 | 0.599 | 0.571 |
| **71** | 1653.9 | 24 | 0.706 | 0.735 | 0.726 | 0.657 |
| **72** | 1653.1 | 32 | 0.704 | 0.754 | 0.745 | 0.705 |
| **73** | 1644.9 | 32 | 0.711 | 0.768 | 0.734 | 0.704 |
| **74** | 1652.8 | 32 | 0.706 | 0.760 | 0.743 | 0.702 |
| **75** | 1653.5 | 32 | 0.706 | 0.756 | 0.756 | 0.699 |
| **76** | 1646.8 | 32 | 0.711 | 0.767 | 0.747 | 0.696 |
| **77** | 1676.6 | 12 | 0.687 | 0.711 | 0.557 | 0.560 |
| **78** | 1677.5 | 12 | 0.684 | 0.709 | 0.547 | 0.574 |
| **79** | 1694.6 | 12 | 0.641 | 0.719 | 0.599 | 0.642 |
| **80** | 1692.6 | 12 | 0.631 | 0.711 | 0.666 | 0.647 |
| **81** | 1695.4 | 12 | 0.648 | 0.713 | 0.565 | 0.550 |
| **82** | 1698.0 | 12 | 0.636 | 0.710 | 0.553 | 0.545 |
| **83** | 1697.2 | 16 | 0.632 | 0.719 | 0.673 | 0.649 |
| **84** | 1644.8 | 32 | 0.715 | 0.756 | 0.774 | 0.762 |
| **85** | 1654.1 | 32 | 0.706 | 0.758 | 0.742 | 0.702 |
| **86** | 1646.8 | 36 | 0.713 | 0.758 | 0.777 | 0.751 |
| ***87*** | ***1642.1*** | 40 | 0.716 | 0.772 | 0.790 | 0.752 |
| **88** | 1653.7 | 40 | 0.712 | 0.759 | 0.776 | 0.759 |
| **89** | 1645.2 | 32 | 0.711 | 0.761 | 0.759 | 0.756 |
| ***90*** | ***1642.0*** | 36 | 0.716 | 0.769 | 0.744 | 0.725 |
| ***91*** | ***1642.8*** | 28 | 0.715 | 0.756 | 0.760 | 0.737 |
| **92** | 1688.7 | 16 | 0.654 | 0.732 | 0.602 | 0.638 |

**Supplementary Table S5. Number of subjects in each immunity subgroup used for odds ratio calculations with serotype 1 as a reference.**

Serotype 1

| Cases | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | Heterologous titres | | | | | |
| Homologous titre | | <10 | [10,20[ | [20,40[ | [40,80[ | [80,160[ | ≥160 |
| | <10 | 96 | 6 | 4 | 7 | 7 | 20 |
| | [10,20[ | 0 | 0 | 0 | 0 | 1 | 2 |
| | [20,40[ | 0 | 0 | 0 | 0 | 2 | 4 |
| | [40,80[ | 0 | 0 | 0 | 0 | 0 | 2 |
| | [80,160[ | 0 | 6 | 0 | 0 | 0 | 1 |
| | ≥160 | 0 | 0 | 1 | 0 | 0 | 1 |
| Non cases | | | | | | | |
| | | Heterologous titres | | | | | |
| Homologous titre | | <10 | [10,20[ | [20,40[ | [40,80[ | [80,160[ | ≥160 |
| | <10 | 488 | 10 | 15 | 34 | 41 | 77 |
| | [10,20[ | 0 | 0 | 0 | 1 | 5 | 25 |
| | [20,40[ | 0 | 1 | 4 | 1 | 3 | 25 |
| | [40,80[ | 0 | 0 | 2 | 1 | 0 | 24 |
| | [80,160[ | 0 | 0 | 1 | 1 | 0 | 15 |
| | ≥160 | 0 | 5 | 11 | 6 | 9 | 57 |

**Supplementary Table S6. Number of subjects in each immunity subgroup used for odds ratio calculations with serotype 2 as a reference.**

Serotype 2

| Cases | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | Heterologous titres | | | | | |
| Homologous titre | | <10 | [10,20[ | [20,40[ | [40,80[ | [80,160[ | ≥160 |
| | <10 | 38 | 2 | 0 | 2 | 2 | 3 |
| | [10,20[ | 0 | 1 | 0 | 2 | 2 | 3 |
| | [20,40[ | 0 | 0 | 0 | 1 | 0 | 3 |
| | [40,80[ | 0 | 0 | 0 | 0 | 0 | 1 |
| | [80,160[ | 0 | 0 | 0 | 0 | 0 | 3 |
| | ≥160 | 0 | 0 | 0 | 0 | 0 | 0 |
| Non cases | | | | | | | |
| | | Heterologous titres | | | | | |
| Homologous titre | | <10 | [10,20[ | [20,40[ | [40,80[ | [80,160[ | ≥160 |
| | <10 | 488 | 6 | 12 | 21 | 10 | 15 |
| | [10,20[ | 4 | 0 | 2 | 5 | 5 | 22 |
| | [20,40[ | 4 | 0 | 2 | 4 | 6 | 24 |
| | [40,80[ | 6 | 0 | 3 | 0 | 1 | 25 |
| | [80,160[ | 17 | 10 | 2 | 0 | 0 | 15 |
| | ≥160 | 12 | 25 | 25 | 13 | 8 | 70 |

**Supplementary Table S7. Number of subjects in each immunity subgroup used for odds ratio calculations with serotype 3 as a reference.**

Serotype 3

Cases

| Homologous titre \ Heterologous titres | <10 | [10,20[ | [20,40[ | [40,80[ | [80,160[ | ≥160 |
|---|---|---|---|---|---|---|
| <10 | 9 | 0 | 0 | 0 | 1 | 0 |
| [10,20[ | 0 | 0 | 0 | 1 | 1 | 2 |
| [20,40[ | 0 | 0 | 0 | 0 | 0 | 3 |
| [40,80[ | 0 | 0 | 0 | 0 | 0 | 1 |
| [80,160[ | 0 | 0 | 0 | 0 | 0 | 0 |
| ≥160 | 0 | 0 | 0 | 0 | 0 | 0 |

Non cases

| Homologous titre \ Heterologous titres | <10 | [10,20[ | [20,40[ | [40,80[ | [80,160[ | ≥160 |
|---|---|---|---|---|---|---|
| <10 | 488 | 9 | 11 | 21 | 19 | 17 |
| [10,20[ | 0 | 1 | 5 | 8 | 15 | 32 |
| [20,40[ | 0 | 1 | 4 | 4 | 6 | 45 |
| [40,80[ | 3 | 0 | 2 | 1 | 1 | 27 |
| [80,160[ | 3 | 3 | 4 | 0 | 0 | 27 |
| ≥160 | 3 | 6 | 14 | 12 | 7 | 64 |

**Supplementary Table S8. Number of subjects in each immunity subgroup used for odds ratio calculations with serotype 4 as a reference.**

Serotype 4

| Cases | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | Heterologous titres | | | | | |
| Homologous titre | | <10 | [10,20[ | [20,40[ | [40,80[ | [80,160[ | ≥160 |
| | <10 | 12 | 0 | 0 | 2 | 0 | 4 |
| | [10,20[ | 0 | 0 | 0 | 0 | 0 | 1 |
| | [20,40[ | 0 | 0 | 0 | 0 | 1 | 0 |
| | [40,80[ | 0 | 0 | 0 | 0 | 0 | 1 |
| | [80,160[ | 0 | 0 | 0 | 0 | 0 | 0 |
| | ≥160 | 0 | 0 | 0 | 0 | 0 | 0 |
| Non cases | | | | | | | |
| | | Heterologous titres | | | | | |
| Homologous titre | | <10 | [10,20[ | [20,40[ | [40,80[ | [80,160[ | ≥160 |
| | <10 | 488 | 4 | 8 | 15 | 39 | 86 |
| | [10,20[ | 5 | 1 | 1 | 1 | 1 | 40 |
| | [20,40[ | 7 | 4 | 0 | 1 | 1 | 20 |
| | [40,80[ | 14 | 6 | 2 | 0 | 0 | 17 |
| | [80,160[ | 1 | 5 | 3 | 1 | 0 | 12 |
| | ≥160 | 5 | 1 | 6 | 3 | 1 | 63 |

**Supplementary Table S9. Odds ratio of clinical dengue illness depending on multiple homologous immunity cut-offs per serotype. BIS stands for baseline immune status, as defined in each scenario, and BIS OR is then the Odds Ratio of clinical dengue with each serotype in individuals with antibody tires above a certain threshold compared with the Odds Ratio of children with lower antibody titres.**

| ***DENV1*** | | | ***DENV2*** | | | ***DENV3*** | | | ***DENV4*** | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *Immune defined as having any PRNT50 titre >=10* | | | | | | | | | | | |
| | ***Immune*** | ***Naive*** | | ***Immune*** | ***Naive*** | | ***Immune*** | ***Naive*** | | ***Immune*** | ***Naive*** |
| *Cases* | *20* | *133* | *Cases* | *16* | *47* | *Cases* | *8* | *10* | *Cases* | *3* | *18* |
| *Non cases* | *197* | *665* | *Non cases* | *310* | *552* | *Non cases* | *298* | *565* | *Non cases* | *222* | *640* |
| *BIS OR* | *0.508 (0.309-0.834)* | | *BIS OR* | *0.606 (0.338-1.087)* | | *BIS OR* | *1.517 (0.592-3.884)* | | *BIS OR* | *0.4805 (0.140-1.647)* | |
| *p-value* | ***0.0074*** | | *p-value* | ***0.0930*** | | *p-value* | ***0.3852*** | | *p-value* | ***0.2435*** | |
| ***Immune defined as having any PRNT50 titre >= 40*** | | | | | | | | | | | |
| | ***Immune*** | ***Naive*** | | ***Immune*** | ***Naive*** | | ***Immune*** | ***Naive*** | | ***Immune*** | ***Naive*** |
| *Cases* | *11* | *140* | *Cases* | *4* | *59* | *Cases* | *1* | *17* | *Cases* | *1* | *20* |
| *Non cases* | *132* | *730* | *Non cases* | *232* | *630* | *Non cases* | *177* | *686* | *Non cases* | *134* | *722* |
| *BIS OR* | *0.708 (0.216-0.777)* | | *BIS OR* | *0.1841 (0.066-0.512)* | | *BIS OR* | *0.228 (0.030-1.725)* | | *BIS OR* | *0.269 (0.036-2.024)* | |
| *p-value* | ***0.0063*** | | *p-value* | ***0.0012*** | | *p-value* | ***0.1521*** | | *p-value* | ***0.2025*** | |
| ***Immune defined as having any PRNT50 titre >= 80*** | | | | | | | | | | | |
| | ***Immune*** | ***Naive*** | | ***Immune*** | ***Naive*** | | ***Immune*** | ***Naive*** | | ***Immune*** | ***Naive*** |
| *Cases* | *9* | *142* | *Cases* | *3* | *60* | *Cases* | *0* | *18* | *Cases* | *0* | *21* |
| *Non cases* | *105* | *757* | *Non cases* | *197* | *665* | *Non cases* | *143* | *720* | *Non cases* | *95* | *761* |
| *BIS OR* | *0.457 (0.226-0.924)* | | *BIS OR* | *0.169 (0.052-0.544)* | | *BIS OR* | *0.136 (0.008-2.265)* | | *BIS OR* | *0.185 (0.011-3.086)* | |
| *p-value* | ***0.0292*** | | *p-value* | ***0.0029*** | | *p-value* | ***0.1643*** | | *p-value* | ***0.2402*** | |
| ***Immune defined as having any PRNT50 titre >= 160*** | | | | | | | | | | | |
| | ***Immune*** | ***Naive*** | | ***Immune*** | ***Naive*** | | ***Immune*** | ***Naive*** | | ***Immune*** | ***Naive*** |
| *Cases* | *2* | *149* | *Cases* | *0* | *63* | *Cases* | *0* | *18* | *Cases* | *0* | *21* |
| *Non cases* | *88* | *774* | *Non cases* | *153* | *709* | *Non cases* | *106* | *757* | *Non cases* | *73* | *783* |
| *BIS OR* | *0.118 (0.029-0.485)* | | *BIS OR* | *0.0364 (0.002-0.592)* | | *BIS OR* | *0.192 (0.011-3.213)* | | *BIS OR* | *0.248 0.015-4.134)* | |
| *p-value* | ***0.0025*** | | *p-value* | ***0.0199*** | | *p-value* | ***0.2511*** | | *p-value* | ***0.3313*** | |