Spatiotemporal Variability in Dengue Transmission Intensity in Jakarta, Indonesia

Authors: Megan O'Driscoll[1*], Natsuko Imai[1], Neil M. Ferguson[1], Sri Rezeki Hadinegoro[2], Hindra Irawan Satari[2], Clarence C. Tam[3,4], Ilaria Dorigatti[1].

Author Affiliations:

1. MRC Centre for Global Infectious Disease Analysis, Department of Infectious Disease Epidemiology, Imperial College London, London, United Kingdom

2. Department of Child Health, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia

3. Saw Swee Hock School of Public Health, National University of Singapore and National University Health System, Singapore

4. London School of Hygiene & Tropical Medicine, London, United Kingdom.

Corresponding author:

Megan O'Driscoll

Email: m.odriscoll@imperial.ac.uk

Abstract

Background

Approximately 70% of the global burden of dengue disease occurs on the Asian continent, where many large urban centres provide optimal environments for sustained endemic transmission and periodic epidemic cycles. Jakarta, the capital of Indonesia, is a densely populated megacity with hyperendemic dengue transmission. Characterization of the spatiotemporal distribution of dengue transmission intensity is of key importance for optimal implementation of novel control and prevention programmes, including vaccination. In this paper we use mathematical models to provide the first detailed description of spatial and temporal variability in dengue transmission in Jakarta.

Methodology/Principal Findings

We applied catalytic models in a Bayesian framework to age-stratified dengue case notification data to estimate dengue force of infection and reporting probabilities in 42 subdistricts of Jakarta. The model was fit to yearly and average annual data covering a 10-year period between 2008 and 2017. We estimated a long-term average annual transmission intensity of 13.0% (95%CrI: 12.9-13.1%) per year in Jakarta province, ranging from 9.0% (95%CrI: 7.7-10.3%) to 16.4% (95%CrI: 15.3-17.4%) across subdistricts. Annual average transmission intensity in Jakarta province during the 10-year period ranged from 1.2% (95%CrI: 1.1-1.3%) in 2017 to 12.4% (95%CrI: 12.1-12.8%) in 2016.

Conclusions/Significance

While the absolute number of dengue case notifications cannot be relied upon as a measure of endemicity, the age-distribution of reported dengue cases provides valuable insights into the underlying nature of transmission. Our estimates from yearly and average annual case notification data represent the first detailed estimates of dengue transmission intensity in Jakarta's subdistricts, which will be important to consider when assessing the population-level impact and cost-effectiveness of potential control and prevention programmes in Jakarta province, such as the controlled release of *Wolbachia*-carrying mosquitoes and vaccination.

Introduction

Dengue is the most rapidly expanding mosquito-borne viral disease (1). Increased globalization and rapid urbanization continue to facilitate the geographic expansion of the mosquito vector and virus in tropical regions, where the frequency and magnitude of dengue epidemics has increased dramatically in the past 40 years (2). Approximately 70% of the global burden of dengue disease occurs on the Asian continent (3), where many large urban centres provide optimal environments for sustained endemic transmission and periodic epidemic cycles.

Indonesia reports the highest number of dengue haemorrhagic fever (DHF) cases in the WHO Southeast Asia Region (1), though experts acknowledge that case numbers are largely under-reported and that reporting practices vary substantially by region (4). The 1997 World Health Organization (WHO) case definitions are used for dengue reporting in Indonesia, where only dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) are notifiable. A cluster-design cross-sectional seroprevalence survey conducted in 2014 estimated an average annual force of infection of 0.140 (95%CI: 0.133-0.147) in urban populations of Indonesia (5). Jakarta, the capital of Indonesia, is a densely populated megacity with endemic transmission of all 4 dengue serotypes and cyclical epidemics every 3-5 years (6,7). Current control strategies in Jakarta focus on the removal of mosquito breeding sites by the Mosquito Nest Eradication Program (Pemberantasan Sarang Nyamuk (PSN)), as well as the periodic use of chemical insecticides for vector management (8).

The characterization of spatial and temporal variability in dengue transmission intensity has become increasingly important in recent years as a way to inform optimal implementation of novel vector control and prevention strategies, including the release of *Wolbachia*-infected mosquitoes and vaccination. The most recent WHO guidelines for use of the world's first dengue vaccine, CYD-TDV (also known as Dengvaxia), recommend a 'test-before-vaccination' approach with serological testing of individuals prior to vaccination (9), thus presenting significant financial and logistical challenges for the implementation of vaccination campaigns. While the implementation of individual-based screening and vaccination programmes may not be feasible at the national-level for many countries, geographically targeted interventions implemented at a sub-national level may present a more realistic and cost-effective option in specific settings. Dengue force of infection, a key measure of transmission intensity, provides valuable insights into the age-related risk of infection and population immunity dynamics. In many dengue endemic countries, routinely collected case notifications are often the only available source of data with which to assess dengue transmission intensity. Though the reliability of dengue case notification data based on clinical diagnoses can vary due to non-specific clinical manifestations caused by dengue and

other vector-borne infections, analysis of the relationship between age and disease incidence can provide valuable insights into the underlying nature and intensity of dengue transmission (10).

The age-related patterns of dengue incidence obtained from reported surveillance data can be attributed to the transmission setting and multiple other factors, including the complex immunological interactions of the four dengue virus serotypes, reporting practices, health-seeking behaviour and surveillance capacities. A large proportion of dengue infections result in mild or no symptoms and infection with any one serotype is thought to provide long-term immunity to the same serotype and a short-lived period of cross-protection against infections with heterologous serotypes (11,12). Severe dengue disease is often, but not always, associated with secondary infections through an immunopathological phenomenon known as antibody-dependent enhancement (ADE), whereby pre-existing anti-DENV antibodies enhance disease severity in secondary heterologous infections (13). Due to cross-reactivity of dengue antibodies in current serological assays, less is known about tertiary and quaternary infections (14) which are thought to cause less symptomatic disease than primary or secondary infections (15). For this reason, most mathematical models of dengue transmission assume clinical protection upon secondary infection (16).

Here we apply catalytic models (10) to provide the first detailed description of spatial and temporal variability in dengue transmission intensity in Jakarta, Indonesia. We estimated dengue transmission intensity and reporting probabilities from age-stratified case notification data in 42 subdistricts of Jakarta over a 10-year period between 2008 and 2017. These estimates can inform the implementation of future control and preventative programmes.

Methods

Data:

In Jakarta province, cases of dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) are both notified as DHF to the Ministry of Health in Jakarta. These publicly available data are reported from public and private hospitals as well as *puskesmas* (primary healthcare centres) (17). Laboratory confirmation of dengue is uncommon, with diagnoses predominantly based on clinical criteria and basic haematology results (18). Age-stratified case notification data were collated for the 44 subdistricts (administrative level 3) of Jakarta for the years 2008-2017 (17). DHF cases reported in children <1 year old were excluded from our analyses due to the existence of maternal antibodies which could have potentially predisposed some infants to symptomatic or severe disease (19). Since the life expectancy in Indonesia is approximately 70 years (20), we assumed that cases reported in the age

group ≥75 occurred in individuals aged 75-80. We used population age structure data from the Jakarta Open Data website (21) and from the Ministry of National Development Planning (22). The population age structure for Jakarta province was available for 2010 and 2014 (22) and the population age structure at the subdistrict-level was available for the years 2014-2016 (21). From the provincial-level population age structure for 2010 and 2014, we derived average annual age group-specific rates of population change, which were applied to the 2014 subdistrict-level age structures to obtain approximate subdistrict age structures for the years 2010-2013. In the absence of population data before 2010 and after 2016, we assumed the same population age structure observed in 2010 for the years 2008 and 2009 and the same age structure observed in 2016 for the year 2017 across all subdistricts. The yearly population age structures derived for each subdistrict from the available data are given in Supplementary file (S2). The yearly total case numbers and incidence rates of hospitalized DHF for Jakarta province used in this analysis are reported in Table 1 and data by subdistrict are available in Tables S1 and S2 (SI Text). Between 2008 and 2017, over 200,000 hospitalized cases of DHF were reported in Jakarta, which corresponds to an average incidence of 2.07 per 1,000 persons per year. Figure 1 shows the average age-specific incidence of hospitalized DHF averaged over the 10-year period, by region and subdistrict. The Thousand Islands/Kepulauan Seribu regency was omitted from subsequent analyses due to sparse case notification data from this regency, a chain of islands in the Java Sea that are predominantly privately owned.

Year	Hospitalized DHF cases	Incidence of hospitalized DHF cases per 1,000
2008	27,656	2.980
2009	27,694	2.984
2010	28,101	3.027
2011	10,552	1.115
2012	11,901	1.234
2013	18,848	1.917
2014	17,916	1.789
2015	11,494	1.128
2016	38,675	3.753
2017	7,870	0.764
2008-2017	200,707	2.069

Table 1. Total hospitalized dengue haemorrhagic fever (DHF) cases and corresponding incidence rates in Jakarta province reported by hospitals to the Jakarta Ministry of Health

Epidemiological surveillance (17). Data at subdistrict-level are provided in Tables S1 and S2 of the Supplementary Information (SI Text).

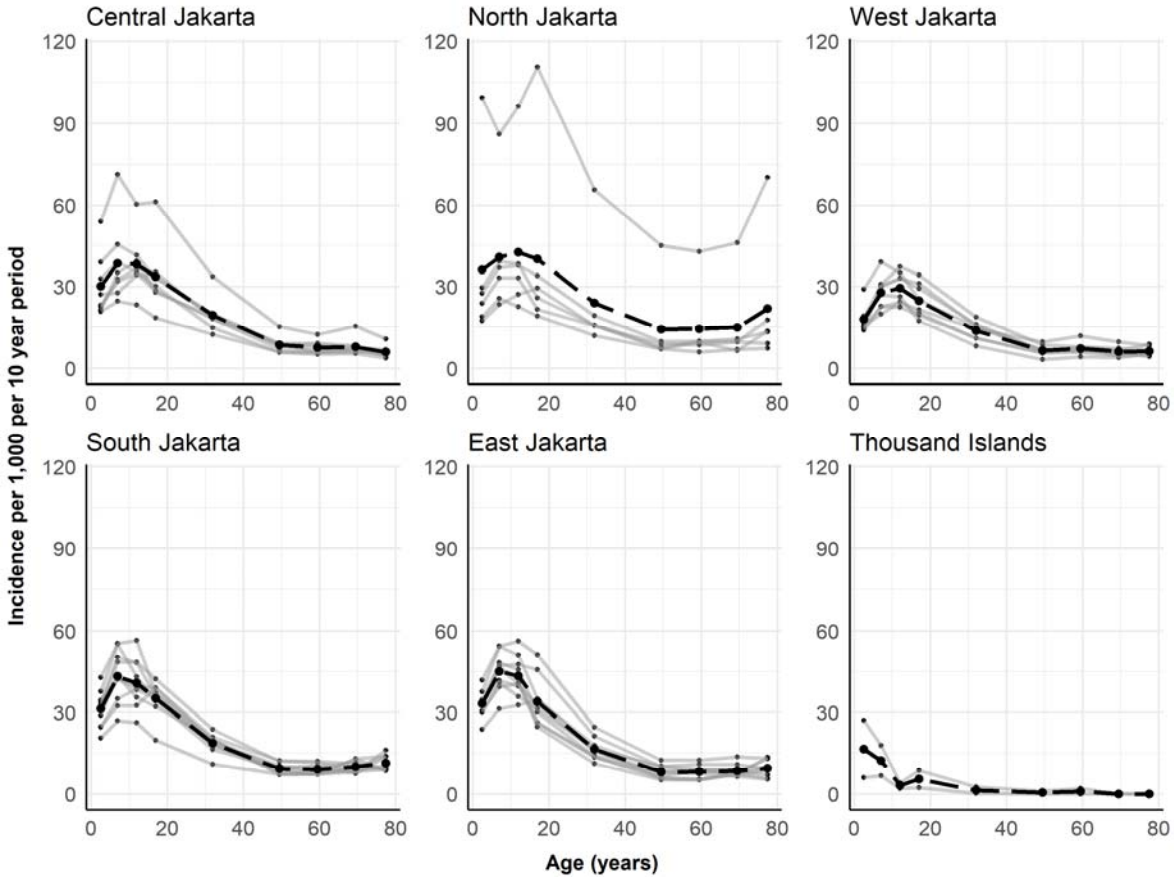

Figure 1. Cumulative age-specific incidence of hospitalized dengue haemorrhagic fever (DHF) cases by region and subdistrict for the 10 year period between 2008 and 2017 in Jakarta province. Grey lines show subdistrict age-distributions and black dashed lines show the average age-distribution of hospitalized DHF cases for the region. Dengue case notification data were obtained from the Jakarta Ministry of Health Epidemiological surveillance system (17). Subdistrict incidence rates and population age structures and are reported in Tables S2 and S3.

Mathematical Models:

In this analysis we apply two mathematical models. Model 1, which assumes time-constant transmission intensity, is fit to age-stratified case data averaged over the entire 10-year period to infer long-term average estimates in transmission intensity. This is done at both province and subdistrict levels. Model 2 allows transmission intensity to vary in time, which we fit to yearly data at both province and subdistrict levels. Both models assume

transmission of all four dengue virus serotypes (6), and that infection with any one serotype provides lifelong homotypic immunity. The models also assume that transmission intensity is age-constant and, due to lack of serotype-specific data, that the four dengue serotypes were transmitted with equal intensity.

Model 1:

Model 1 assumes endemic dengue transmission which is constant in time and age. Under these assumptions the incidence of primary, secondary, tertiary and quaternary infections by age can be calculated as described in detail by Imai et al. (10). The incidence of primary infections in age group *j* is calculated as shown in equation 1:

$$I_1(j) = \int_{a_j}^{a_{j+1}} 4\lambda\left(e^{-\lambda a}\right)^4 da$$

[Equation 1]

Equations for the calculation of the incidence of secondary, tertiary and quaternary infections are given in section 2 of the SI. Here λ denotes the force of infection of each individual serotype, with the total force of infection calculated as four times the serotype-specific force of infection (i.e. 4λ). a_j and a_{j+1} represent the lower and upper bounds of age group *j*. Assuming clinical protection after secondary infection (i.e. that tertiary and quaternary infections are not symptomatic), the average annual incidence of dengue disease per person in age group *j*, *D(j)*, is then calculated as the weighted sum of primary and secondary infection incidence, assuming time-constant reporting rates:

$$D(j) = \frac{\rho}{w(j)}(I_2(j) + \gamma_1(I_1(j)) + \mathrm{B}w(j))$$

[Equation 2]

where ρ denotes the probability that a secondary infection is symptomatic and reported to surveillance, *w(j)* is the width of age group *j*, γ_1 is the probability that a primary infection is reported relative to a secondary infection, and B is the probability of reporting non-dengue illnesses as dengue infections (e.g. due to misdiagnosis). Time-constant basic reproduction numbers (R_0) were calculated from serotype-specific force of infection estimates, λ, under two assumptions (equations shown in section 3.4 of the SI text). Under assumption 1, we assume that all infections (primary to quaternary) contribute to onward transmission; under assumption 2, we assume that only primary and secondary infections are infectious and thus contribute to dengue transmission.

Model 2:

In model 2 we extend model 1 to allow transmission intensity to vary from year to year. In order to estimate the population immune profiles at the beginning of the time period, we assume transmission intensity to have been constant throughout the lifetimes of individuals observed in the first year of our data, i.e. a constant transmission intensity for 80 years prior to and including 2008. The incidence of primary and secondary infections in subsequent years can then be calculated based on the existing immune profiles, the proportion susceptible, S, and monotypic, M, by age, as shown in equations 3-6.

$$S(a,t) = \mathrm{e}^{-4\lambda(t)a}$$

[Equation 3]

$$M(a,t) = 4e^{-3\lambda(t)a} \cdot (1 - e^{-\lambda(t)a})$$

[Equation 4]

$$I_1(a,t) = 4\lambda(t) \cdot S(a,t-1)$$

[Equation 5]

$$I_2(a,t) = 3\lambda(t) \cdot M(a,t-1)$$

[Equation 6]

We fit to each of the 10 years simultaneously, whereby the transmission intensity in each year is dependent on the transmission intensity of all other years. The susceptible and monotypic population proportions are estimated by single years of age to account for ageing of the immune profiles each year. These estimates are then averaged across the age groups of our data and disease incidence is calculated as in Equation 2. Due to the presence of maternal immunity potentially increasing the risk of disease in <1 year olds, the model was fit to case data from 1-80 year olds only. Susceptible and monotypic proportions of 1 year olds were added to the population each year at a rate consistent with having been exposed to the previous year's force of infection.

For both Model 1 and Model 2 we explored two assumptions about the infections that contribute to the observed disease incidence (in this case, hospitalized DHF cases) and defined two model sub-variants, which we denoted S and PS. Under model variant S we assumed that all hospitalized DHF cases were caused by secondary infections (i.e. we set γ1 to zero). Under model variant PS we assumed that hospitalized DHF cases could be

caused by primary or secondary infections, where primary infections were less likely to be symptomatic and reported than secondary infections ($\gamma 1<\rho$).

We used a multinomial log-likelihood (for details see section 3 of the SI), and Markov Chain Monte Carlo (MCMC) methods with a Metropolis-Hastings algorithm for parameter inference. For Model 2 the log-likelihood from each fit was estimated as the sum of yearly multinomial log-likelihoods. We assumed uniform priors on all parameters. Age-specific seroprevalence estimates were obtained using force of infection estimates as detailed in section 3.3 of the SI Text. The proportion of subdistricts reaching 50%, 70% and 90% seroprevalence at 9 years of age were calculated using average force of infection estimates obtained from the fit of model 1 to average annual age-stratified DHF incidence rates from the 10-year period (2008-2017) in Jakarta's subdistricts.

Spatial Analysis:

Spatial autocorrelation of dengue force of infection was assessed using the Moran's I-coefficient and local indicator of spatial association (LISA) metrics. The significance of the Moran's I-coefficient was assessed by a Monte-Carlo permutation test with 1,000 simulations, under the null-hypothesis that subdistrict estimates of dengue force of infection are randomly distributed within the province of Jakarta. Subdistrict population density estimates from the 2010 census, available online (23), were used to assess the relationship between subdistrict population density and the estimated dengue force of infection using a simple linear regression model (full details given in section 3.5 of SI Text).

All analyses were conducted in R statistical software, version 3.4.3 (24).

Results

All parameter estimates and model fits for Jakarta province, obtained using both model variants *S* (assuming all reported hospitalised DHF cases are due to secondary infections) and *PS* (assuming reported hospitalised DHF cases are due to primary and secondary infections), are given in Table S4 and Figures S1 and S2 of the SI Text. Model variants *S* and *PS* produced largely similar estimates, particularly when estimates of the probability of primary infections being reported as DHF cases (γ_1) are negligible. Model variant *PS* was favoured by Deviance Information Criterion (DIC) and therefore for brevity, in the remainder of the manuscript we focus on the results obtained with model variant *PS*. Estimates from model variant *S* are given in the SI Text. All force of infection estimates quoted in this manuscript refer to the total force of infection from all dengue serotypes (i.e. 4λ).

An average annual force of infection of 0.130 (95%CrI: 0.129-0.131) was estimated for Jakarta province between 2008 and 2017 using model 1 variant *PS*. This same model produced estimates of the probability of a dengue infection resulting in a reported hospitalized DHF case (reporting rate for secondary infections, ρ) of 0.077 (95%CrI: 0.076-0.078), with primary infections being 0.002 (95%CrI: 0.001-0.009) times as likely to result as hospitalized DHF (reporting probability, γ_1 relative to ρ) (SI, Table S4). Using model 2, variant PS, the annual average force of infection in Jakarta province varied by year from 0.012 (95%CrI: 0.011-0.013) in 2017 to 0.124 (95%CrI: 0.121-0.128) in 2016 (blue points in Figure 2 and Table S4). The range of spatiotemporal variation is shown in Figure 2, where the green points represent the median annual average force of infection estimates obtained at the subdistrict level.

Figure 3 shows the average annual subdistrict force of infection estimates obtained from the fit of model 1 variant *PS* to data averaged over the 10-year period, 2008-2017. We find that Sawah Besar subdistrict had the lowest average annual transmission intensity, with an average force of infection of 0.090 (95%CrI: 0.077-0.103) per year, while Pasar Rebo experienced the highest average force of infection of 0.163 (95%CrI: 0.153-0.174) per year (see SI Text, Table S5 for full results). Maps of yearly subdistrict force of infection are shown in Supplementary Figure S6. Analysis of spatial autocorrelation of the average annual subdistrict force of infection estimates for the 10-year period using model 1 variant *PS* showed significant spatial clustering of dengue transmission, with a Moran's I-coefficient of 0.29 (p-value=0.002). Significant clustering of high transmission intensity subdistricts was observed in central-southeast Jakarta, predominantly in the region of East Jakarta, while spatial clustering of low transmission intensity subdistricts was observed in the region of Central Jakarta (Figure 3 and Figure S5 in SI Text). Using force of infection estimates from model 1 variant *PS* fit to data averaged over the period 2008-2017 we observed a weak correlation between subdistrict force of infection and population density, with a $6.334e^{-7}$ (95%CI: $-9.262e^{-8}$-$1.359e^{-6}$) average increase in force of infection per unit increase in population density. Population density explained approximately 5% (adjusted R^2=0.049) of the variability in annual average subdistrict force of infection estimates (Figure S8 in SI Text).

Using the average annual force of infection estimates obtained with model 1 variant *PS* from the 10-year period, we derived the expected proportion of seropositive population by age in Jakarta province and estimated the extent to which this proportion would vary between the highest and lowest transmission intensity subdistricts within Jakarta, as shown in Figure 4A. All subdistrict estimates of the proportion of seropositive 9-year olds are given in Supplementary Table S5. At age 9, the expected proportion of seropositive individuals in

Jakarta province is 68.9% (95%CrI: 68.6-69.3) ranging from 55.6% (95%CrI: 50.2-60.4) to 77.1% (95%CrI: 74.8-79.1) across subdistricts. By age 15, this proportion is expected to have risen to 85.8% (95%CrI: 85.5-86.0) for the entire province, ranging from 74.2% (95%CrI: 68.7-78.7) to 91.4% (95%CrI: 89.9-92.7) across subdistricts. Figure 4B shows the expected proportion of subdistricts that reach 50%, 70% and 90% seroprevalence by age. We find that 100% (42/42) of subdistricts in Jakarta are expected to have at least 50% seroprevalence amongst 9 year olds, and 38% (16/42) are expected to have seroprevalence levels above 70% at this age. At age 15, all subdistricts (42/42) are expected to have seroprevalence levels of at least 70%, with 12% (5/42) of subdistricts expected to have seroprevalence levels of 90% or more in this age group.

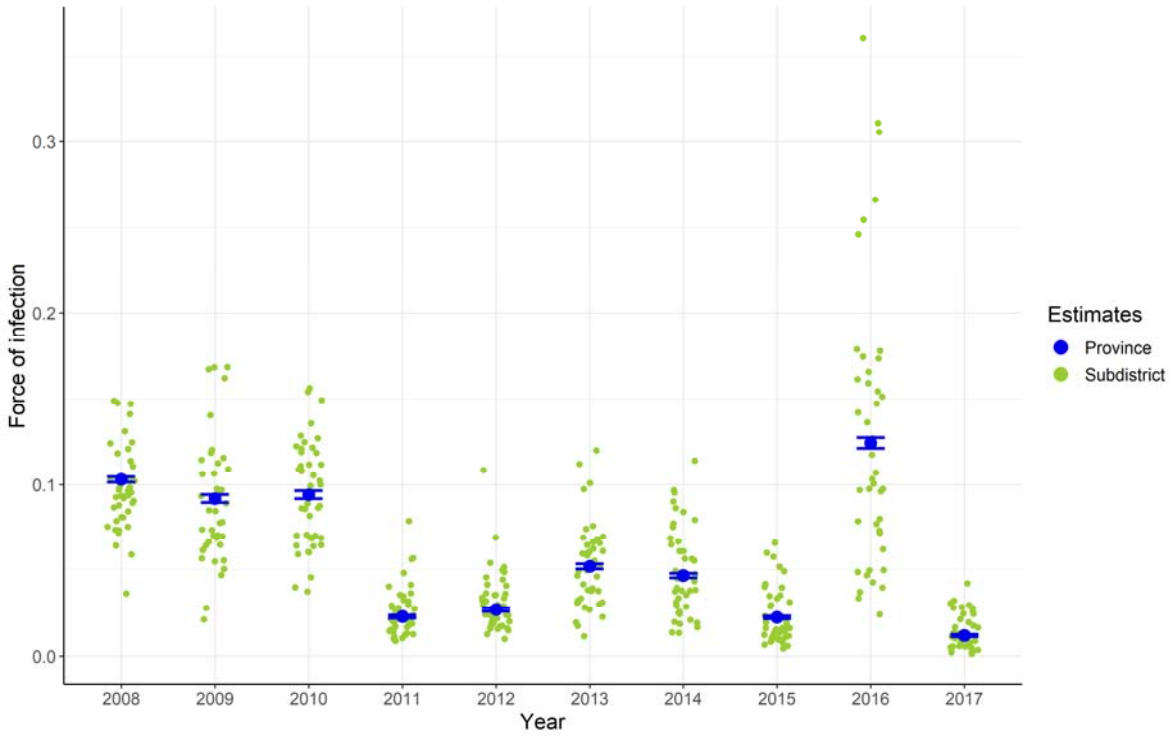

Figure 2. Total force of infection (4λ) estimates obtained from the fit of model 2 variant *PS* (assuming reported hospitalised DHF cases are caused by primary or secondary infections) to annual DHF cases reported between 2008 and 2017. Blue points show the median and 95% credible interval of the estimates obtained for the whole province of Jakarta. Green points represent the yearly median estimates obtained at the subdistrict level. Annual subdistrict parameter estimates are available in S3 Supplementary File.

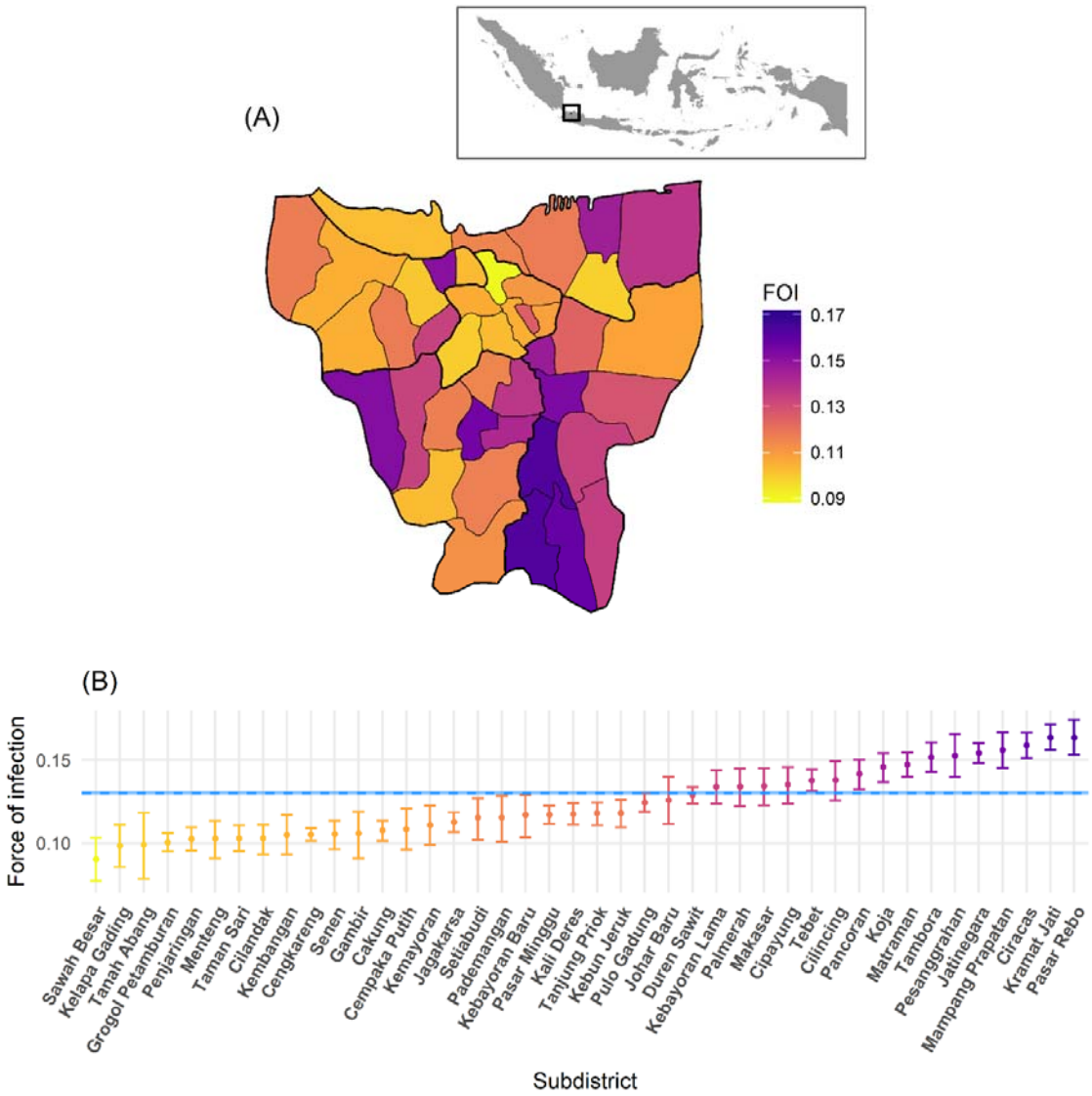

Figure 3. Spatial variation in average annual total dengue force of infection (4λ) estimates in Jakarta obtained from the fit of model 1 variant *PS* (assuming reported hospitalised DHF cases are caused by primary or secondary infections) to average annual hospitalised DHF data reported in 2008-2017. (A) Map of median force of infection estimates per subdistrict with grey panel showing the location of Jakarta in Indonesia; (B) median and 95% credible interval of the estimates reported in panel A. Blue dashed line and shading shows the median and 95% credible interval province-level average annual force of infection in 2008-2017. FOI: force of infection.

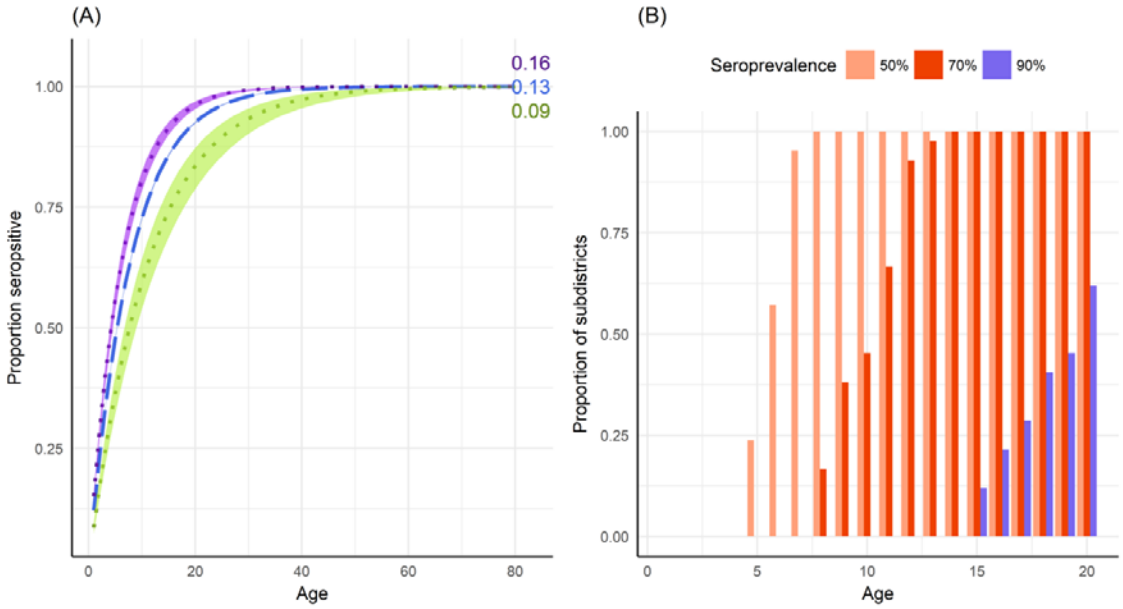

Figure 4. Expected seroprevalence levels in Jakarta province. (A) Expected proportion (median and 95% credible interval) of the population seropositive to dengue by age using the total force of infection (4λ) estimate obtained from the fit of model 1 variant *PS* (assuming all hospitalised DHF cases are caused by primary or secondary infections) to average annual hospitalised DHF data reported in the period 2008-2017 in Jakarta province (blue dashed line); Sawah Besar, the subdistrict with the lowest force of infection estimate (green); and Pasar Rebo, the subdistrict with the highest force of infection estimate (purple). The corresponding average force of infection estimate is given at the end of each line. (B) The proportion of subdistricts (N=42) in Jakarta province that reach at least 50%, 70% and 90% seroprevalence by age, obtained from subdistrict force of infection estimates using model 1 variant *PS* fit to average annual incidence of hospitalised DHF cases reported in the period 2008-2017.

Discussion

We find that the force of infection estimate obtained with model 1 variant *PS* fitted to average annual case notification data reported between 2008 and 2017 in Jakarta province (0.130 (95%CrI: 0.129-0.131)) is similar to the estimate obtained from seroprevalence data collected in 2014 in 30 urban subdistricts of Indonesia (0.14 (95%CI: 0.133-0.147)) (5,25). We observed significant spatiotemporal heterogeneity in force of infection within Jakarta province, with long-term spatial clustering of both high and low transmission intensity subdistricts. Our analysis identified a hot-spot of dengue transmission in the southeast of Jakarta province and clustering of low transmission intensity in the region of Central Jakarta.

Subdistrict population density was found to have a weak association with dengue transmission intensity, explaining approximately 5% of the variation in subdistrict force of infection estimates during the period of 2008-2017, with higher average annual force of infection associated with greater population densities (for details see SI sections 3.5 and Figure S8). Though this association may suggest higher rates of human-vector contact in densely populated areas, numerous other environmental, socioeconomic and behavioural factors not included in this analysis are likely to influence local transmission intensity.

Annual transmission intensity estimates for Jakarta province during 2008-2017 ranged from 0.012 (95%Cr: 0.011-0.013) in 2017 to 0.124 (0.121-0.128) in 2016, with large heterogeneity at the subdistrict level. This temporal variability in annual dengue force of infection means that the expected proportion of dengue-naïve children in any one age group also varies by year which, coupled with complex immunological factors, such as antibody-dependent enhancement, will shape the risk of severe dengue in children in any given year. Results from recent analyses of a longitudinal study conducted in Thailand found a significant cohort effect on the proportion of 9 year olds who were dengue-naïve by study year, with up to a twofold difference in the probability of being dengue-naïve depending on year (26). When assessing the level of dengue transmission from case notification data, it is therefore important to consider data from multiple years in order to obtain reliable long-term estimates of average transmission intensity which will hold relevance for public health policy decision-makers.

Recent studies (27,28) have demonstrated that vaccination campaigns with the CYD-TDV vaccine could potentially increase individual-level risks of disease in low-to-medium transmission intensity settings, highlighting the importance of tailoring control and preventative programmes to the local setting. While the World Health Organization (WHO) initially advised that countries with geographic settings reaching at least 70% seroprevalence by 9 years of age could consider CYD-TDV vaccination (29), recent new data from Sanofi Pasteur (30,31) produced a change in the vaccine recommendations, with CYD-TDV vaccination currently advised only among subjects ≥9 years of age with evidence of a previous dengue infection (9,32). Though temporal variability in force of infection means that the proportion of seropositive individuals in any one age group will also vary by year, our estimates from data averaged across the 10-year period represent long-term averages in transmission intensity. Using these estimates we expect average seroprevalence levels of 59.1% (95%CrI: 58.7-59.4), 78.6% (95%CrI: 78.3-78.9) and 88.8% (95%CrI: 88.6-89.0), in the 5-9, 10-14 and 15-19 age groups, respectively, in Jakarta province. Additionally, we expect every subdistrict in Jakarta to have seroprevalence levels of at least 50% amongst 9 year olds, suggesting that across all subdistricts, at least one in every two 9 year olds that

are serologically screened would be eligible for vaccination. The age-specific seroprevalence estimates presented in this study can inform potential future individual-based serological screening programmes, to determine the proportion of screened individuals that would be eligible for vaccination.

Overall, we find that the *S* and *PS* model variants produce largely similar estimates of average force of infection, except for years when substantial proportions of DHF cases are estimated to be caused by primary infections (γ_1). For these years, as expected, model variant *S* estimates a higher force of infection than model variant *PS*, due to the assumption that all DHF cases have experienced two infections. Further, though we allow post-secondary infections to contribute to transmission, we assumed that they do not cause severe disease. Though post-secondary infections are thought to be largely asymptomatic due to long-term heterotypic immunity, if a considerable proportion of severe dengue cases were being caused by tertiary or quaternary infections (perhaps in older individuals whose cross-protective immunity had waned) our model could potentially underestimate the force of infection. As shown in (14), a low age of seroconversion and a high age of DHF are easier to reconcile when relaxing the assumption of clinical protection after secondary infection, which is important to consider given the high occurrence of post-secondary infections observed in hyperendemic regions of Indonesia (33) as well as the increasing average age of DHF cases that has been observed in the country (34).

There are potential limitations in the assumptions adopted in this analysis which are important to consider when interpreting the estimates obtained with our models. When estimating transmission intensity within administratively-defined boundaries, we inherently assume that cases reported in any one administrative unit were also infected in that same administrative unit, which is less realistic at small administrative levels such as subdistricts. We assumed reporting probabilities to be constant with time and age, though fluctuations in reporting may occur over time due to situational awareness (e.g. during epidemics) or by age if any age-related reporting biases were occuring. Additionally, the parameter results shown in this analysis are estimated assuming no overdispersion in the distribution of dengue cases (i.e. we assume a Poisson distribution for the total number of cases and a multinomial distribution for the age distribution of cases). In exploratory analysis (not shown), we tested the use of overdispersed case distributions (specifically assuming a negative binomial distribution for the total number of cases and a Dirichlet multinomial likelihood for the age-distribution of cases) to more accurately account for uncertainty and widen the confidence intervals around our parameter estimates. However, use of these over-dispersed distributions hindered convergence of our MCMC chains, constraining our model to assume the absence of overdispersion in case distributions. A significant dengue outbreak occurred

in Jakarta in 2016, for which our model could not entirely reproduce the high rates of disease observed in the 10-14 years age group (Figure S2 in the SI Text). It is therefore possible that the transmission intensity estimates produced in this analysis for 2016 underestimated the actual force of infection that year. In addition, dengue transmission in Jakarta has a distinct seasonal pattern, with case numbers typically peaking in March through May, following the rainy season (35). In this analysis we assumed that the force of infection is constant within each year, ignoring intra-annual variability and thus producing average annual transmission intensity estimates. Long-term estimates of transmission intensity, however, will hold relevance to decisions when considering the implementation of future control and prevention programmes.

In conclusion, using publicly available data on DHF cases reported in Jakarta in the 10-year period of 2008-2017, we have presented the first detailed analysis of the spatiotemporal variation in dengue transmission intensity conducted to date in Jakarta province. This study highlights the importance of estimating dengue transmission intensity from the analysis of age-stratified dengue case notification data rather than inferring it from the absolute number of cases, which can often be misleading. The estimates presented in this study will provide invaluable insights into the potential impact and cost-effectiveness of future control and preventative programmes, including vaccination with current or future dengue vaccines, and the use of the *Wolbachia* technology, in the province of Jakarta.

Funding

We acknowledge grant funding support from the Medical Research Council (Centre grant MR/R015600/1 - NMF, NI, MO'D, ID), the Imperial College Junior Research Fellowship Scheme (ID), the National Institute of General Medical Science MIDAS initiative (grant 5U01GM110721 - NMF) and the Bill and Melinda Gates Foundation (grant OPP1092240 – NMF, NI, MO'D, ID). The funders had no role in study design, data analysis, decision to publish, or preparation of the manuscript.

Author Contributions

MO'D, ID, NI and NMF developed the analysis plan. MO'D conducted the analysis and wrote the paper. ID, NI and NMF supervised the project. MO'D, ID, NI, NMF, CCT, HIS, SRH contributed to the interpretation of the results and critical review of the manuscript.

Data Availability

All data used in this analysis are reported in the tables and figures of the manuscript and supporting information or are publicly available online.

Competing Interests

SRH and HIS have been clinical trial and/or study investigators for, and received associated payments from, Sanofi Pasteur, a company involved in the development of dengue vaccines.

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Supporting Information

1. DHF case notification data reported in Jakarta.

Table S1. Annual number of hospitalized DHF cases per subdistrict between 2008 and 2017, excluding cases in infants <1 year. Available online at (17).

Subdistrict	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2008-2017
Cakung	1,608	1,618	1,353	439	494	1,137	611	462	1,556	434	9,712
Cempaka Putih	602	640	586	187	160	221	188	133	445	100	3,262
Cengkareng	704	378	1,176	367	453	676	856	592	3157	418	8,777
Cilandak	764	705	692	187	262	407	406	178	502	56	4,159
Cilincing	535	1,040	730	390	368	412	404	464	975	280	5,598
Cipayung	467	520	677	225	314	542	446	284	1227	225	4,927
Ciracas	478	657	535	217	333	451	416	257	1071	196	4,611
Duren Sawit	2,015	1,557	1,595	677	655	1,113	911	639	1905	499	11,566
Gambir	272	196	239	99	112	146	150	102	307	62	1,685
Grogol Petamburan	620	444	482	163	288	460	622	257	794	135	4,265
Jagakarsa	674	834	754	207	398	650	664	414	1,642	277	6,514
Jatinegara	960	842	877	274	282	528	456	229	1,196	331	5,975
Johar Baru	405	375	538	134	150	139	153	86	360	80	2,420
Kali Deres	383	181	540	224	303	409	530	379	1,820	251	5,020
Kebayoran Baru	430	516	505	161	240	356	395	247	810	149	3,809
Kebayoran Lama	961	871	894	345	428	447	527	288	1127	264	6,152
Kebun Jeruk	911	764	749	200	191	218	260	130	432	92	3,947
Kelapa Gading	712	1,210	856	448	371	1,311	1,248	1,452	1,093	191	8,892
Kemayoran	772	782	845	303	294	518	583	303	795	151	5,346
Kembangan	399	437	704	207	253	415	519	192	641	106	3,873
Kep. Seribu Selatan	0	2	2	12	8	4	8	13	10	5	64
Kep. Seribu Utara	1	5	1	0	4	0	3	3	7	0	24
Koja	737	1,137	896	488	386	377	443	385	1,153	290	6,292
Kramat Jati	810	643	786	258	332	495	481	253	1,188	237	5,483
Makasar	537	458	523	228	269	359	389	261	793	228	4,045
Mampang Prapatan	616	552	431	105	154	311	299	146	638	114	3,366
Matraman	681	706	736	211	198	258	225	153	659	130	3,957
Menteng	331	220	254	91	95	126	112	62	228	54	1,573
Pademangan	301	362	391	213	198	272	238	127	552	109	2,763
Palmerah	711	565	429	258	360	457	255	154	586	168	3,943
Pancoran	663	716	655	120	192	409	357	233	557	97	3,999
Pasar Minggu	1,383	1,257	1,070	318	408	634	787	337	1,383	322	7,899
Pasar Rebo	327	490	451	288	388	417	348	176	926	207	4,018
Penjaringan	596	592	522	314	331	556	571	169	1104	146	4,901

Pesanggrahan	305	419	448	120	175	339	388	176	722	109	3,201
Pulo Gadung	959	1,089	827	271	436	793	482	344	1,454	428	7,083
Sawah Besar	332	325	373	170	149	174	162	101	466	75	2,327
Senen	452	385	392	127	115	194	137	69	284	40	2,195
Setiabudi	382	335	367	164	135	244	166	65	440	74	2,372
Taman Sari	314	325	347	139	143	157	157	75	318	37	2,012
Tambora	428	366	375	181	207	252	282	221	531	127	2,970
Tanah Abang	233	200	311	133	175	226	210	105	484	98	2,175
Tanjung Priok	1,109	1,135	1,286	616	455	746	627	564	1,525	307	8,370
Tebet	776	843	901	273	239	492	444	214	812	171	5,165
Total Cases in Jakarta	*27,656*	*27,694*	*28,101*	*10,552*	*11,901*	*18,848*	*17,916*	*11,494*	*38,675*	*7,870*	*200,707*

Table S2. Annual subdistrict incidence rates (IR) per 1,000 population, between 2008 and 2017, excluding cases in infants <1 year. Case data are available online at (17). Calculated annual age-structures are reported in Supplementary File S2.

Subdistrict	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2008-2017
Cakung	3.610	3.632	3.037	0.964	1.062	2.395	1.261	0.917	3.071	0.857	2.081
Cempaka Putih	7.981	8.484	7.769	2.326	1.875	2.447	1.973	1.398	4.459	1.002	3.971
Cengkareng	1.459	0.784	2.438	0.756	0.927	1.375	1.730	1.189	6.137	0.813	1.761
Cilandak	4.014	3.704	3.636	0.967	1.334	2.040	2.004	0.873	2.428	0.271	2.127
Cilincing	1.438	2.794	1.961	1.041	0.976	1.085	1.057	1.187	2.432	0.698	1.467
Cipayung	2.157	2.402	3.128	1.016	1.386	2.340	1.885	1.149	4.831	0.886	2.118
Ciracas	1.924	2.645	2.154	0.853	1.280	1.696	1.530	0.920	3.816	0.698	1.752
Duren Sawit	5.598	4.326	4.431	1.835	1.734	2.878	2.302	1.575	4.700	1.231	3.061
Gambir	3.474	2.503	3.052	1.185	1.262	1.553	1.511	1.029	3.070	0.620	1.926
Grogol Petamburan	2.858	2.047	2.222	0.743	1.300	2.055	2.750	1.142	3.551	0.604	1.927
Jagakarsa	2.394	2.962	2.678	0.725	1.374	2.213	2.230	1.332	5.159	0.870	2.194
Jatinegara	3.437	3.014	3.140	0.957	0.961	1.757	1.483	0.734	3.856	1.067	2.041
Johar Baru	3.730	3.454	4.956	1.160	1.224	1.073	1.121	0.623	2.499	0.555	2.040
Kali Deres	1.029	0.486	1.451	0.599	0.805	1.081	1.393	0.968	4.668	0.644	1.312
Kebayoran Baru	3.100	3.720	3.640	1.141	1.672	2.439	2.663	0.827	5.419	0.997	2.562
Kebayoran Lama	3.429	3.108	3.190	1.212	1.481	1.524	1.771	1.935	3.686	0.864	2.220
Kebun Jeruk	2.977	2.496	2.447	0.648	0.614	0.695	0.822	0.405	1.329	0.283	1.271
Kelapa Gading	5.749	9.771	6.912	3.572	2.922	10.199	9.592	11.039	8.213	1.435	6.941
Kemayoran	3.960	4.011	4.334	1.459	1.334	2.223	2.372	1.208	3.104	0.590	2.460
Kembangan	1.636	1.791	2.886	0.842	1.021	1.661	2.062	0.732	2.426	0.401	1.546
Kep. Seribu Selatan	0.000	0.239	0.239	1.367	0.869	0.416	0.796	1.271	0.911	0.455	0.656

Kep. Seribu Utara	0.080	0.399	0.080	0.000	0.290	0.000	0.199	0.196	0.436	0.000	0.168
Koja	2.450	3.780	2.979	1.610	1.264	1.225	1.429	1.207	3.592	0.903	2.044
Kramat Jati	3.144	2.496	3.051	0.978	1.230	1.792	1.704	0.876	4.126	0.823	2.022
Makasar	2.947	2.513	2.870	1.222	1.408	1.837	1.947	1.265	3.858	1.109	2.098
Mampang Prapatan	4.419	3.960	3.092	0.742	1.073	2.137	2.026	0.974	4.196	0.750	2.337
Matraman	4.146	4.299	4.481	1.252	1.146	1.457	1.241	0.837	3.596	0.709	2.316
Menteng	4.761	3.164	3.653	1.227	1.205	1.510	1.271	0.699	2.472	0.585	2.055
Pademangan	1.969	2.368	2.558	1.381	1.272	1.732	1.502	0.785	3.443	0.680	1.769
Palmerah	3.434	2.728	2.072	1.234	1.707	2.147	1.187	0.710	2.721	0.780	1.872
Pancoran	4.526	4.888	4.472	0.807	1.273	2.673	2.300	1.463	3.466	0.604	2.647
Pasar Minggu	4.965	4.512	3.841	1.125	1.423	2.181	2.670	1.122	4.555	1.061	2.745
Pasar Rebo	1.770	2.652	2.441	1.523	2.006	2.109	1.722	0.847	4.414	0.987	2.047
Penjaringan	2.100	2.086	1.839	1.096	1.144	1.905	1.938	0.554	3.699	0.489	1.685
Pesanggrahan	1.425	1.958	2.093	0.552	0.794	1.516	1.711	0.757	3.023	0.456	1.429
Pulo Gadung	3.659	4.155	3.156	1.009	1.584	2.813	1.671	1.187	4.972	1.464	2.567
Sawah Besar	3.183	3.116	3.576	1.529	1.262	1.392	1.228	0.766	3.507	0.564	2.012
Senen	4.612	3.929	4.000	1.216	1.038	1.655	1.108	0.560	2.199	0.310	2.063
Setiabudi	3.650	3.201	3.507	1.542	1.250	2.224	1.490	0.585	3.873	0.651	2.197
Taman Sari	2.622	2.714	2.897	1.146	1.164	1.262	1.247	0.598	2.557	0.298	1.650
Tambora	1.684	1.440	1.475	0.705	0.799	0.964	1.069	0.837	2.041	0.488	1.150
Tanah Abang	1.708	1.466	2.280	0.916	1.136	1.387	1.223	0.614	2.678	0.542	1.395
Tanjung Priok	2.997	3.068	3.476	1.650	1.208	1.963	1.636	1.456	3.886	0.782	2.212
Tebet	3.608	3.920	4.190	1.248	1.075	2.176	1.932	0.925	3.452	0.727	2.325
Average IR in Jakarta	*2.980*	*2.984*	*3.027*	*1.115*	*1.234*	*1.917*	*1.789*	*1.128*	*3.753*	*0.764*	*2.069*

2. Population age-structures

Table S3. Average population age-structures calculated for the period 2008-2017. Yearly population age-structures used are given in Supplementary file S2.

Subdistrict	1-4	5-9	10-14	15-19	20-44	45-54	55-64	65-74	>75	Total
Cakung	43,697	44,254	38,036	36,500	223,198	51,694	26,377	7,617	1,934	473,307
Cempaka Putih	6,458	6,957	6,772	6,810	37,785	11,736	6,295	3,118	1,302	87,233
Cengkareng	44,150	43,581	37,950	39,562	236,817	54,006	26,165	8,674	2,531	493,436
Cilandak	15,313	16,317	15,381	15,427	88,278	25,632	13,151	6,077	2,464	198,040
Cilincing	35,918	35,656	31,501	31,366	182,056	37,736	19,207	7,011	1,847	382,298
Cipayung	20,706	21,032	19,130	18,701	105,033	27,634	13,895	4,665	1,288	232,084
Ciracas	23,107	23,194	20,578	20,496	120,456	31,309	17,573	5,633	1,453	263,799
Duren Sawit	31,740	32,991	29,257	28,360	172,836	44,272	27,216	12,582	3,275	382,529
Gambir	6,119	6,612	6,606	6,839	38,769	11,940	7,714	3,595	1,771	89,965
Grogol Petamburan	17,173	16,753	14,119	15,488	103,285	26,255	16,376	8,730	3,202	221,381
Jagakarsa	26,108	26,692	23,462	23,584	134,865	34,350	17,986	6,907	1,906	295,860
Jatinegara	24,706	25,004	22,471	22,690	130,494	36,601	21,121	9,337	3,383	295,807
Johar Baru	9,943	10,991	10,365	10,238	55,403	15,359	8,449	3,593	1,260	125,601
Kali Deres	33,901	34,381	30,143	32,642	181,921	41,197	17,602	6,013	1,890	379,690
Kebayoran Baru	11,953	12,669	12,044	12,291	69,573	21,463	11,799	5,221	2,268	159,281
Kebayoran Lama	22,318	22,909	20,557	21,168	125,618	34,262	18,443	8,511	2,763	276,549
Kebun Jeruk	27,209	25,284	22,077	23,838	147,968	35,568	20,546	8,723	2,758	313,971
Kelapa Gading	9,263	9,405	8,310	9,123	57,593	16,028	11,222	5,427	1,653	128,024
Kemayoran	17,748	19,207	18,418	17,810	98,254	28,287	15,698	7,412	2,638	225,472
Kembangan	21,776	21,294	18,059	19,848	118,779	28,145	16,102	5,972	1,810	251,785
Kep. Seribu Selatan	890	953	981	817	4,021	1,005	513	245	66	9,491
Kep. Seribu Utara	1,327	1,349	1,500	1,348	5,876	1,550	768	290	143	14,151
Koja	28,869	27,723	23,866	24,607	145,298	33,302	17,185	6,378	1,751	308,979
Kramat Jati	24,057	24,246	21,089	20,756	123,257	32,979	17,576	6,881	2,166	273,007
Makasar	16,706	16,885	14,949	14,980	87,556	23,820	12,792	4,700	1,300	193,688
Mampang Prapatan	12,060	12,351	10,963	11,293	66,329	18,069	9,168	3,628	1,155	145,016
Matraman	13,950	14,394	13,230	13,202	75,391	23,547	12,758	5,565	2,147	174,184

Menteng	5,867	6,225	6,238	6,483	34,212	10,819	6,723	2,804	1,256	80,627
Pademangan	13,037	13,311	11,556	11,955	73,183	18,063	9,953	4,239	1,373	156,670
Palmerah	17,718	17,749	15,308	16,755	96,943	25,674	13,555	5,760	2,168	211,630
Pancoran	12,890	12,888	11,157	11,345	69,903	18,787	9,758	4,615	1,441	152,784
Pasar Minggu	24,457	25,147	21,749	21,935	133,332	34,592	18,127	7,971	2,506	289,816
Pasar Rebo	17,273	17,712	15,585	15,032	89,757	23,259	12,517	4,097	1,149	196,381
Penjaringan	23,682	24,065	21,419	22,051	136,324	32,828	19,765	8,456	2,969	291,559
Pesanggrahan	19,137	19,482	17,658	17,233	102,305	25,700	14,673	6,146	1,681	224,015
Pulo Gadung	22,129	23,079	20,725	20,841	123,240	36,079	18,559	9,328	3,555	277,535
Sawah Besar	8,320	8,913	8,548	8,923	52,275	15,612	10,096	4,836	2,147	119,670
Senen	8,386	9,036	8,667	8,923	49,616	14,585	8,708	3,733	1,501	113,155
Setiabudi	8,366	8,909	8,023	8,325	48,588	14,227	7,735	3,316	1,293	108,782
Taman Sari	8,603	8,639	7,977	9,284	54,698	15,672	10,469	5,051	2,398	122,791
Tambora	20,131	20,846	18,267	20,299	120,254	30,732	17,707	7,592	2,960	258,788
Tanah Abang	12,550	13,324	12,495	12,680	68,930	20,035	11,010	4,670	1,856	157,550
Tanjung Priok	32,161	32,505	28,097	29,623	176,861	43,971	23,948	9,504	2,866	379,536
Tebet	17,554	18,059	17,090	17,625	97,205	29,860	16,406	7,488	3,098	224,385
Total (Jakarta Province)	819,426	832,973	742,373	759,096	4,464,335	1,158,241	633,406	262,111	88,341	9,760,302

3. Mathematical Models

3.1 Model 1 – Incidence of infections

The incidence of primary, secondary, tertiary and quaternary infections within each age group *j* are given by the following equations (Equations 1.1-1.4).

$$I_1(j) = \int_{a_j}^{a_{j+1}} 4\lambda\left(e^{-\lambda a}\right)^4 da$$

[1.1]

$$I_2(j) = 4\int_{a_j}^{a_{j+1}} 3\lambda(1-e^{-\lambda a})\left(e^{-\lambda a}\right)^3 da$$

[1.2]

$$I_3(j) = 4\int_{a_j}^{a_{j+1}} 3\lambda(1-e^{-\lambda a})^2\left(e^{-\lambda a}\right)^2 da$$

[1.3]

$$I_4(j) = 4\int_{a_j}^{a_{j+1}} \lambda\left(1-e^{-\lambda a}\right)^3 e^{-\lambda a} da$$

[1.4]

The average annual incidence of dengue disease per person in age group *j*, *D(j),* is then calculated as the weighted sum of primary and secondary infections (Equation 2):

$$D(j) = \frac{\rho}{w(j)}(I_2(j) + \gamma_1(I_1(j)) + \mathrm{B}w(j))$$

[2]

Here λ is the age- and time-constant force of infection of each dengue serotype, a_j and a_{j+1} are the lower and upper bounds of age group *j*, respectively. ρ is the probability that a secondary infection results in a detectable dengue case (baseline reporting rate), *w(j)* is the width of age group *j*, γ_1 is the probability that a primary infection is detected relative to a secondary infection, and *B* is the probability of reporting non-dengue illnesses as dengue due to misdiagnosis (baseline non-dengue reporting). The total force of infection is then calculated as four times the serotype-specific force of infection (i.e. 4λ). All parameters were given uniform priors.

3.2 Likelihood function

The expected number of cases in age group j, C_j, is given by:

$$C_j = D(j)n(j)$$

[3]

Where *D(j)* is the expected disease incidence in age group *j*, and *n(j)* is the population size of age group *j*.

We assumed that the total number of cases per year across all ages, N, was Poisson distributed (Equation 4):

$$P(\mu = N) = \frac{\mu^N e^{-\mu}}{N!}$$

[4]

Where μ is the total expected number of cases across all age groups (i.e. ΣC_j). We assumed that the number of cases reported in each age group were multinomially distributed and so the full log-likelihood is given by:

$$\ln L_j = \sum [\ln(p_j) y_j] + N \ln(\mu) - \mu - \ln(N!)$$

[5]

Where p_j is the expected proportion of cases in one age group relative to the total number of cases across all age groups, (i.e. $C_j / \Sigma_j C_j$), and y_j is the observed number of cases in age group *j*. For Model 2 the log-likelihood was simply calculated as the sum of yearly log-likelihoods.

3.3 Seropositive proportion of the population

The proportion of the population seropositive to at least one dengue serotype by age is determined by the force of infection, *λ*. Given a total force of infection of *4λ* (assuming equal transmissibility across serotypes), the expected proportion of the population seropositive to dengue by age *a*, *p(a)*, is defined by the catalytic model as shown in Equation 6.

$$p(a) = 1 - e^{(-4\lambda a)}$$

[6]

3.4 Basic Reproduction Number

Assuming that dengue force of infection was constant in time and equally transmissible across all 4 serotypes, we calculated the basic reproduction number of each serotype, R_0, under two assumptions. Under assumption 1, we assumed that all infections (primary-quaternary) are equally infectious, with no cross-immunity between serotypes, shown in Equation 7:

$$R_0 = \frac{1}{1 - \int_{a_j}^{a_{j+1}} f(a)[1 - e^{-\lambda a}]da}$$

[7]

Where *f(a)* is the proportion of the population in age group a, $[1-e^{-\lambda a}]$ is the proportion of the population seropositive to one serotype at age *a*, and a_j and a_{j+1} are the lower and upper bounds of age group *j*.

Under assumption 2, we assume that only primary and secondary infections are infectious and contribute to onward transmission. The basic reproduction number for any one serotype is then given by:

$$R_0 = \frac{1}{\int_{a_j}^{a_{j+1}} f(a)[e^{-\lambda a} + (n-1)(1 - e^{-\lambda a})]da}$$

[8]

Where *f(a)* is the proportion of the population in age group *a*, $e^{-\lambda a}$ is the proportion seronegative at age a, n is the number of serotypes in circulation (4 in this case), $[1-e^{-\lambda a}]$ is the proportion seropositive at age *a*, and a_j and a_{j+1} are the lower and upper bounds of age group *j*.

3.5 Linear regression for prediction of force of infection

A simple linear regression model was used to determine the relationship between subdistrict force of infection and population density, as follows:

$$Y = \beta_1 + \beta_2 X + \varepsilon$$

[9]

Where *Y* is the force of infection (4λ), *X* is the population density, β_1 is the intercept, β_2 is the slope, and ε is the error term, which was assumed to be Normally distributed.

4. Results

4.1 Jakarta province: parameter estimates and model fits from averaged (Model 1) and yearly (Model 2) data

Table S4. Median parameter estimates, 95% credible intervals (CrI) and DIC values obtained from the fit of models 1 and 2 (with sub-variants S and PS) to averaged and yearly data reported in the period 2008-2017 in Jakarta province.

		Parameter Values median and (95% CrI's)			
		Model1 - S	*Model1 - PS*	*Model2 - S*	*Model2 - PS*
Average annual force of infection estimates (4λ)	2008*	-	-	0.119 (0.118-0.120)	0.103 (0.101-0.105)
	2009	-	-	0.112 (0.110-0.114)	0.092 (0.089-0.094)
	2010	-	-	0.116 (0.114-0.118)	0.094 (0.092-0.096)
	2011	-	-	0.026 (0.025-0.027)	0.023 (0.022-0.024)
	2012	-	-	0.031 (0.030-0.033)	0.027 (0.026-0.028)
	2013	-	-	0.065 (0.063-0.066)	0.052 (0.051-0.054)
	2014	-	-	0.057 (0.055-0.058)	0.047 (0.045-0.048)
	2015	-	-	0.025 (0.024-0.026)	0.022 (0.021-0.023)
	2016	-	-	0.157 (0.155-0.160)	0.124 (0.121-0.128)
	2017	-	-	0.012 (0.011-0.013)	0.012 (0.011-0.013)
	2008-2017**	0.130 (0.129-0.131)	0.130 (0.129-0.131)	-	-
Reporting parameters	rho	0.077 (0.076-0.078)	0.077 (0.076-0.078)	0.118 (0.116-0.119)	0.118 (0.116-0.120)
	Gamma1	-	0.002 (0.001-0.009)	-	0.146 (0.134-0.159)
	Base	0.010 (0.010-0.010)	0.010 (0.010-0.010)	0.001 (0.001-0.001)	0.001 (0.001-0.001)
	DIC	705,596.309	705,598.373	708,530.400	708,120.900

* The average annual force of infection estimates for Model2 in 2008 assume a constant force of infection throughout the lifetime of individuals, i.e. these values represent the average annual force of infection for 1928-2008.

** The average annual force of infection estimates for Model 1 assume a constant force of infection throughout the lifetime of individuals, i.e. assuming transmission was constant between 1928 and 2017.

Figure S1. Fit of model 1 variants *S* (orange line and ribbon indicating median and 95% credible intervals) and *PS* (green line and ribbon indicating median and 95% credible intervals) to average annual (2008-2017) age-stratified DHF incidence rates reported in Jakarta province (black points and bars, indicating mean and 95% confidence intervals). Confidence intervals around the reported DHF incidence rates were computed using the binomial distribution.

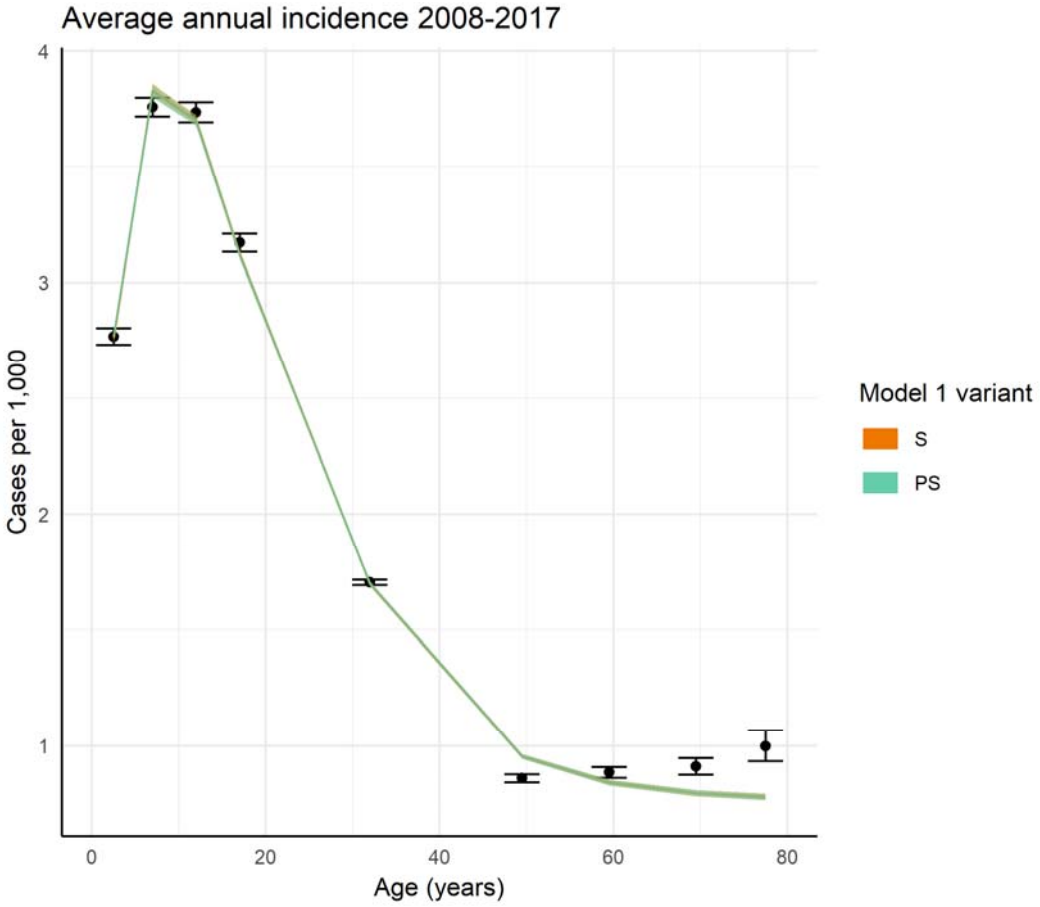


Figure S2. Fit of model 2 variants *S* (orange line and ribbon indicating median and 95% credible intervals) and *PS* (green line and ribbon indicating median and 95% credible intervals) to yearly (2008-2017) age-stratified DHF incidence rates reported in Jakarta province (black points and bars, indicating mean and 95% confidence intervals). Confidence intervals around the reported DHF incidence rates were computed using the binomial distribution.

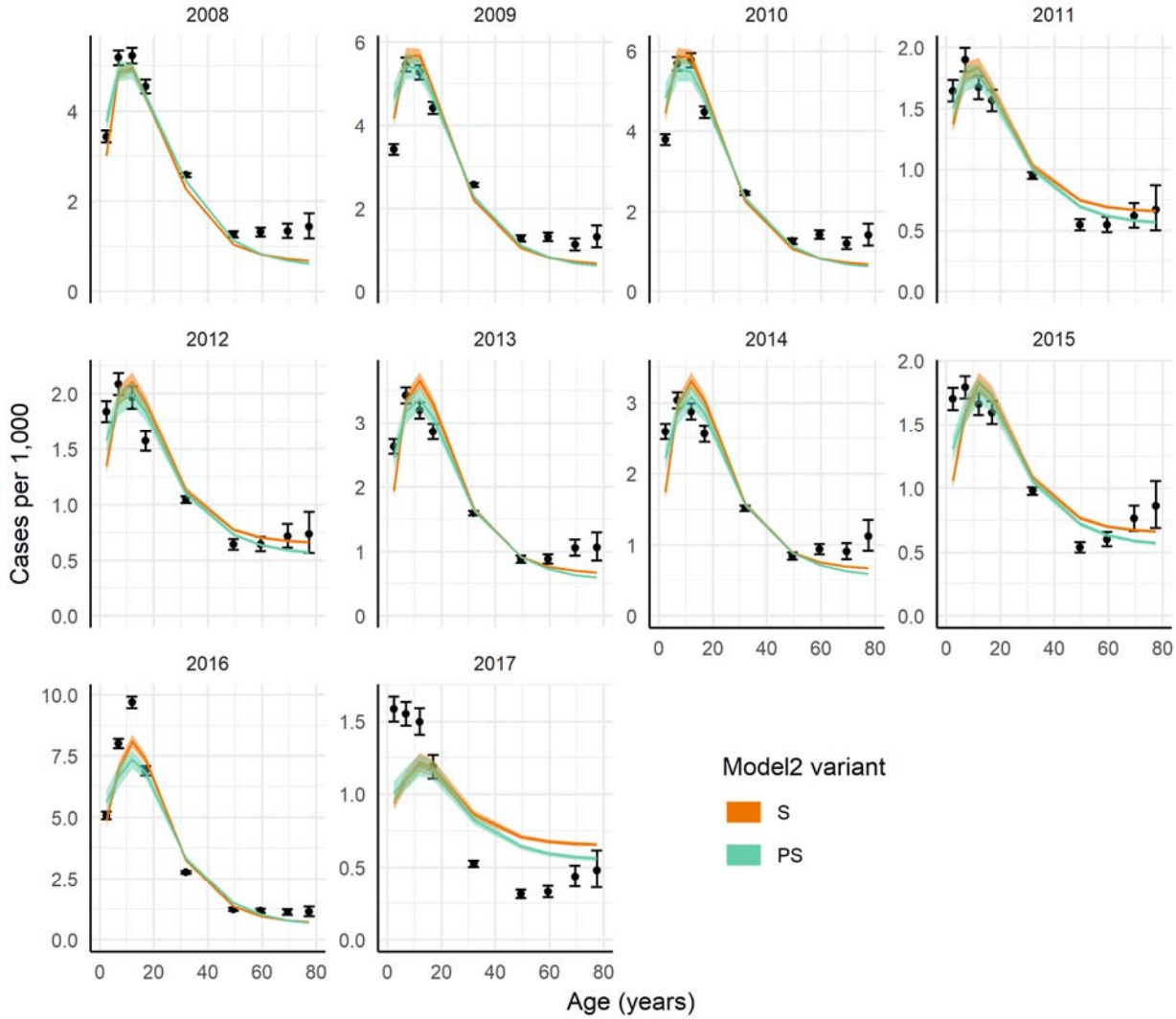


Figure S3. Total number of observed and predicted hospitalized DHF cases by year. The expected number of cases by year estimated by model 2 versions S and PS are shown in green and orange bars, respectively, with 95% credible intervals. Confidence intervals around the observed DHF incidence rates were computed using the binomial distribution.

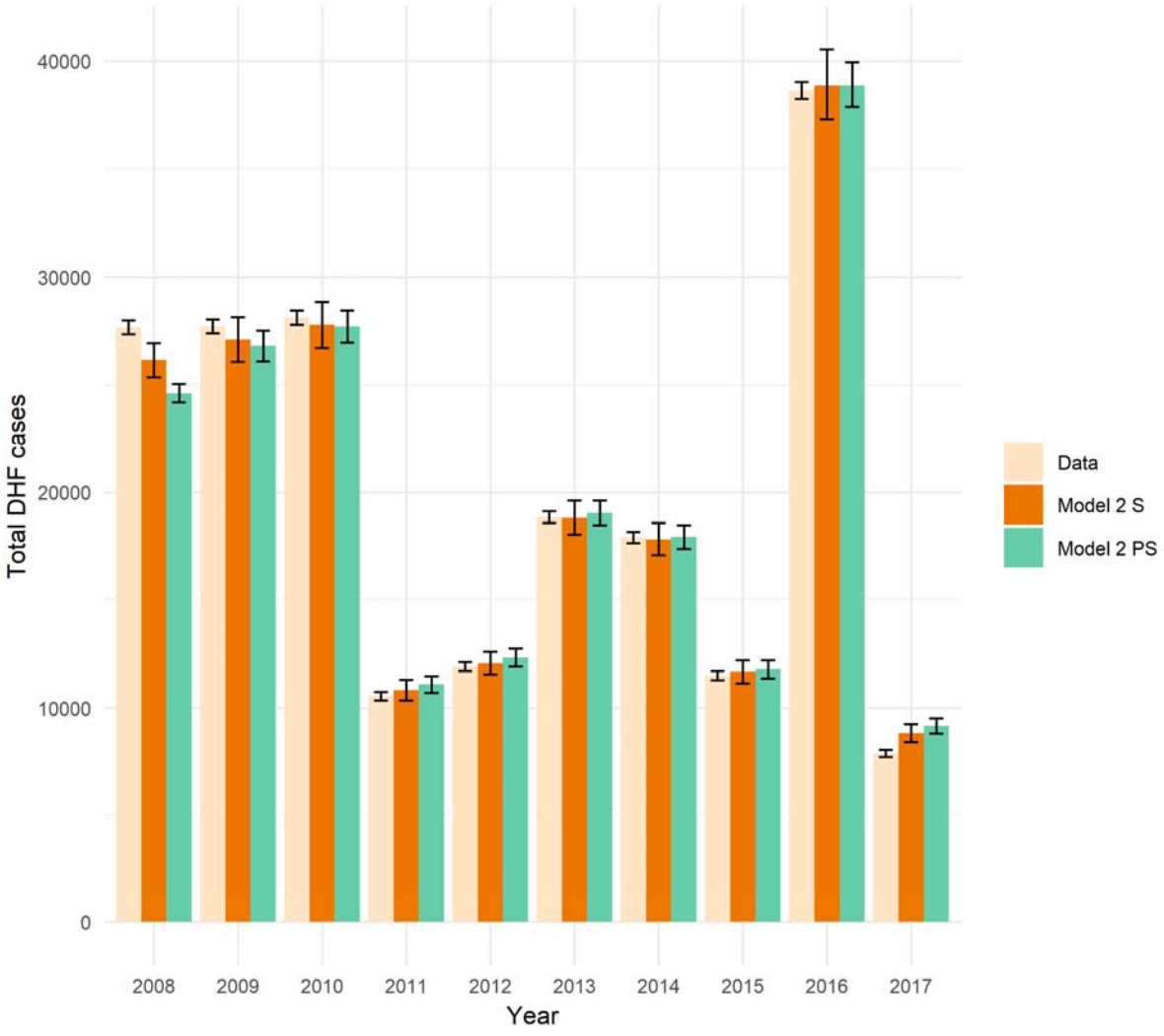


Table S5. Estimated total force of infection, basic reproduction numbers, the proportion of seropositive children at 9 years of age obtained by fitting model 1 variant PS to average annual (2008-2017) DHF data reported in Jakarta's subdistricts, and subdistrict population density. The basic reproduction number (R_0) was estimated under 2 assumptions: under assumption 1 we assume that primary to quaternary infections are equally infectious; under assumption 2 we assume that only primary and secondary infections are infectious and thus contribute to onward transmission. The subdistrict population density estimates are reported online (23).

Subdistrict	Total force of infection, 4λ, (median and 95%CrI)	Proportion of 9 year olds seropositive (median and 95%CrI)	R_0 [assumption 1] (median and 95%CrI)	R_0 [assumption 2] (median and 95%CrI)	Population density per km^2
Cakung	0.108 (0.101-0.113)	0.621 (0.598-0.640)	1.961 (1.892-2.020)	3.112 (2.940-3.261)	12,362
Cempaka Putih	0.108 (0.096-0.121)	0.623 (0.578-0.662)	2.099 (1.950-2.249)	3.490 (3.105-3.877)	18,223
Cengkareng	0.105 (0.102-0.109)	0.612 (0.599-0.625)	1.948 (1.910-1.989)	3.097 (2.999-3.200)	19,589
Cilandak	0.103 (0.093-0.111)	0.604 (0.568-0.632)	2.004 (1.893-2.099)	3.243 (2.958-3.488)	10,685
Cilincing	0.138 (0.126-0.149)	0.711 (0.677-0.739)	2.265 (2.131-2.392)	3.866 (3.535-4.176)	8,923
Cipayung	0.135 (0.124-0.146)	0.704 (0.671-0.730)	2.286 (2.154-2.405)	3.919 (3.593-4.208)	8,215
Ciracas	0.159 (0.151-0.166)	0.761 (0.743-0.776)	2.600 (2.506-2.692)	4.702 (4.474-4.924)	15,137
Duren Sawit	0.129 (0.124-0.134)	0.687 (0.671-0.700)	2.288 (2.224-2.346)	3.944 (3.785-4.090)	17,637
Gambir	0.106 (0.091-0.119)	0.614 (0.558-0.657)	2.122 (1.933-2.291)	3.576 (3.078-4.021)	10,438
Grogol Petamburan	0.100 (0.095-0.106)	0.595 (0.574-0.615)	2.019 (1.952-2.089)	3.307 (3.131-3.490)	20,539
Jagakarsa	0.113 (0.107-0.118)	0.637 (0.617-0.656)	2.046 (1.981-2.110)	3.325 (3.162-3.485)	12,304
Jatinegara	0.154 (0.148-0.160)	0.75 (0.736-0.764)	2.610 (2.533-2.689)	4.731 (4.544-4.920)	25,865
Johar Baru	0.126 (0.111-0.140)	0.678 (0.633-0.716)	2.238 (2.070-2.410)	3.821 (3.395-4.252)	49,162
Kali Deres	0.118 (0.111-0.124)	0.653 (0.632-0.673)	2.061 (1.993-2.134)	3.383 (3.209-3.567)	13,881
Kebayoran Baru	0.117 (0.103-0.129)	0.651 (0.605-0.687)	2.202 (2.035-2.353)	3.760 (3.329-4.147)	11,163
Kebayoran Lama	0.134 (0.123-0.144)	0.701 (0.671-0.726)	2.366 (2.237-2.490)	4.169 (3.841-4.480)	15,157
Kebun Jeruk	0.118 (0.109-0.126)	0.655 (0.627-0.679)	2.154 (2.054-2.249)	3.632 (3.374-3.874)	19,434
Kelapa Gading	0.098 (0.086-0.111)	0.588 (0.537-0.632)	2.024 (1.867-2.185)	3.327 (2.912-3.752)	9,607
Kemayoran	0.111 (0.099-0.123)	0.631 (0.589-0.668)	2.085 (1.948-2.223)	3.432 (3.083-3.781)	30,198
Kembangan	0.105 (0.093-0.117)	0.611 (0.567-0.651)	1.984 (1.855-2.120)	3.192 (2.859-3.539)	10,814
Koja	0.146 (0.137-0.154)	0.731 (0.708-0.750)	2.394 (2.289-2.490)	4.185 (3.930-4.420)	25,195
Kramat Jati	0.164 (0.156-0.171)	0.771 (0.754-0.786)	2.667 (2.572-2.764)	4.843 (4.618-5.073)	20,671
Makasar	0.134 (0.123-0.145)	0.702 (0.669-0.729)	2.323 (2.187-2.450)	4.028 (3.689-4.342)	8,751

Mampang Prapatan	0.156 (0.145-0.167)	0.754 (0.729-0.777)	2.607 (2.472-2.743)	4.759 (4.423-5.090)	17,927
Matraman	0.147 (0.140-0.154)	0.734 (0.716-0.750)	2.559 (2.466-2.650)	4.625 (4.396-4.848)	30,203
Menteng	0.103 (0.091-0.113)	0.603 (0.557-0.639)	2.045 (1.900-2.175)	3.351 (2.978-3.687)	10,506
Pademangan	0.115 (0.101-0.128)	0.646 (0.597-0.685)	2.117 (1.952-2.268)	3.533 (3.108-3.919)	12,239
Palmerah	0.134 (0.122-0.145)	0.701 (0.666-0.729)	2.347 (2.200-2.480)	4.112 (3.741-4.444)	26,998
Pancoran	0.142 (0.132-0.150)	0.721 (0.696-0.741)	2.446 (2.330-2.551)	4.352 (4.063-4.611)	16,703
Pasar Minggu	0.117 (0.112-0.123)	0.651 (0.634-0.668)	2.131 (2.068-2.195)	3.559 (3.397-3.719)	13,345
Pasar Rebo	0.164 (0.153-0.174)	0.771 (0.748-0.791)	2.644 (2.517-2.773)	4.797 (4.493-5.103)	14,599
Penjaringan	0.103 (0.096-0.109)	0.603 (0.577-0.626)	1.984 (1.906-2.063)	3.196 (2.994-3.400)	8,461
Pesanggrahan	0.153 (0.140-0.166)	0.747 (0.716-0.775)	2.542 (2.386-2.704)	4.569 (4.185-4.962)	15,678
Pulo Gadung	0.124 (0.119-0.130)	0.674 (0.657-0.689)	2.265 (2.197-2.332)	3.903 (3.730-4.072)	17,506
Sawah Besar	0.090 (0.077-0.103)	0.556 (0.502-0.604)	1.923 (1.769-2.080)	3.050 (2.650-3.464)	18,817
Senen	0.105 (0.096-0.114)	0.613 (0.580-0.640)	2.057 (1.950-2.156)	3.387 (3.108-3.643)	21,710
Setiabudi	0.115 (0.102-0.127)	0.646 (0.601-0.681)	2.165 (2.004-2.307)	3.665 (3.250-4.029)	14,558
Taman Sari	0.103 (0.095-0.111)	0.603 (0.575-0.631)	2.091 (1.994-2.195)	3.509 (3.251-3.787)	24,062
Tambora	0.152 (0.143-0.161)	0.745 (0.723-0.764)	2.611 (2.493-2.728)	4.826 (4.527-5.121)	44,200
Tanah Abang	0.099 (0.078-0.118)	0.59 (0.506-0.654)	1.950 (1.723-2.168)	3.092 (2.515-3.646)	14434
Tanjung Priok	0.118 (0.111-0.124)	0.654 (0.631-0.673)	2.136 (2.054-2.209)	3.578 (3.367-3.764)	16850
Tebet	0.138 (0.131-0.144)	0.711 (0.693-0.727)	2.448 (2.364-2.532)	4.365 (4.155-4.574)	22167

4.2. Maps of subdistrict locations, spatial autocorrelation & annual subdistrict transmission intensity

Figure S4. Map of Jakarta province with subdistrict and region locations.

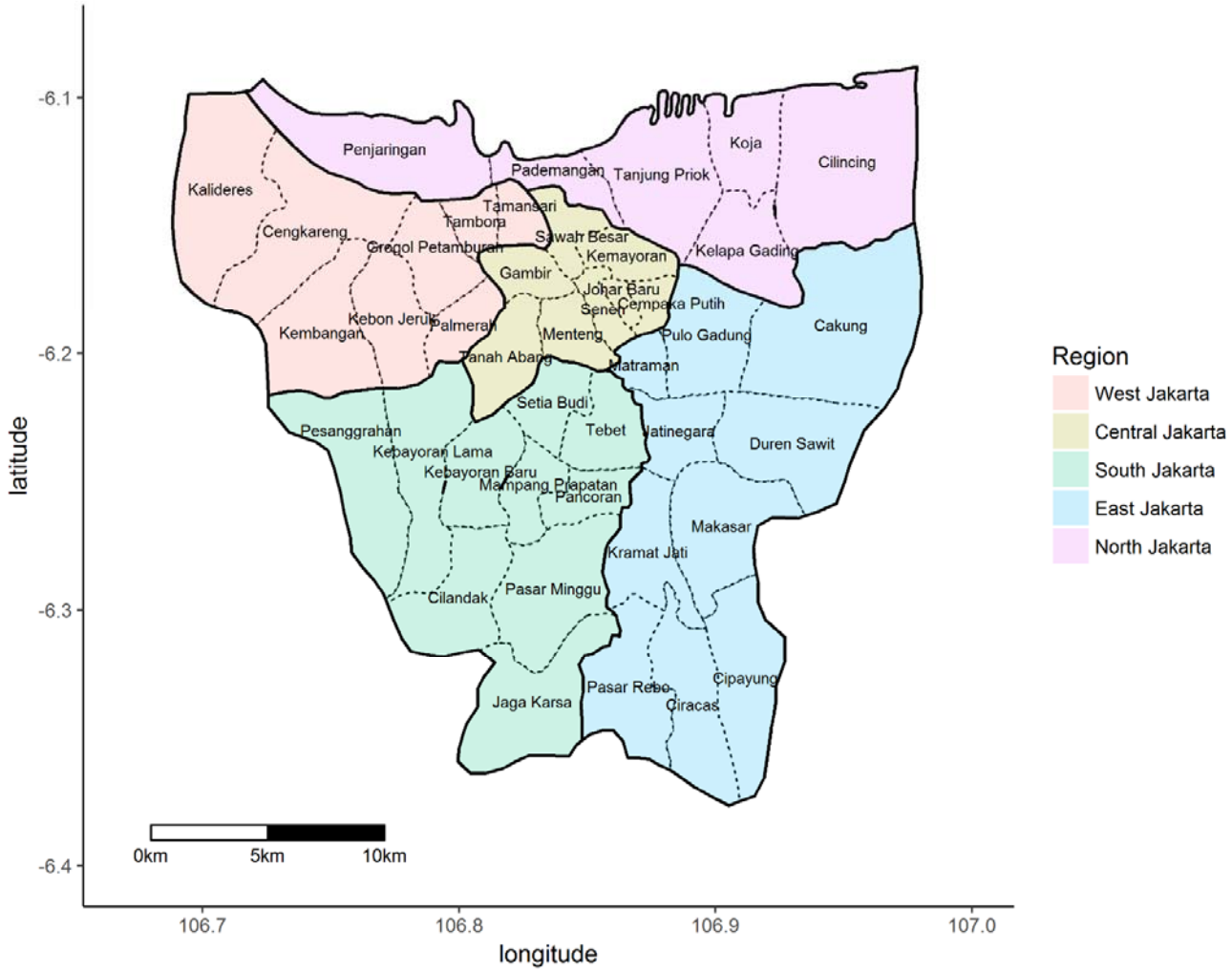


Figure S5. Map of local indicators of spatial association (LISA) for subdistrict total force of infection (4λ) estimates. Red colour indicates spatial clustering of median transmission intensity estimates obtained from the fit of model variant PS to average annual (2008-2017) age-stratified DHF incidence data reported in Jakarta's subdistricts.

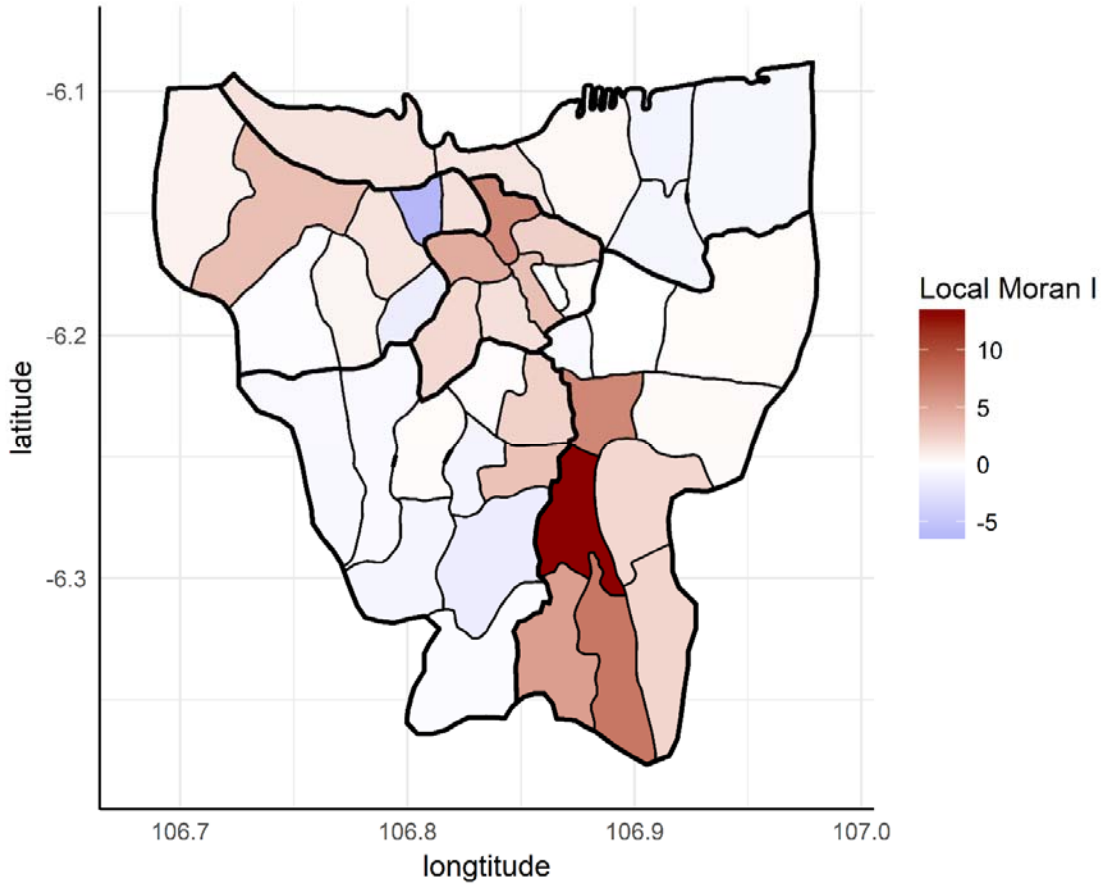


Figure S6. Spatial distribution of median total transmission intensity (4λ) estimates obtained from the fit of model 2 variant *PS* to yearly age-stratified DHF incidence rates reported between 2008 and 2017 in Jakarta's subdistricts.

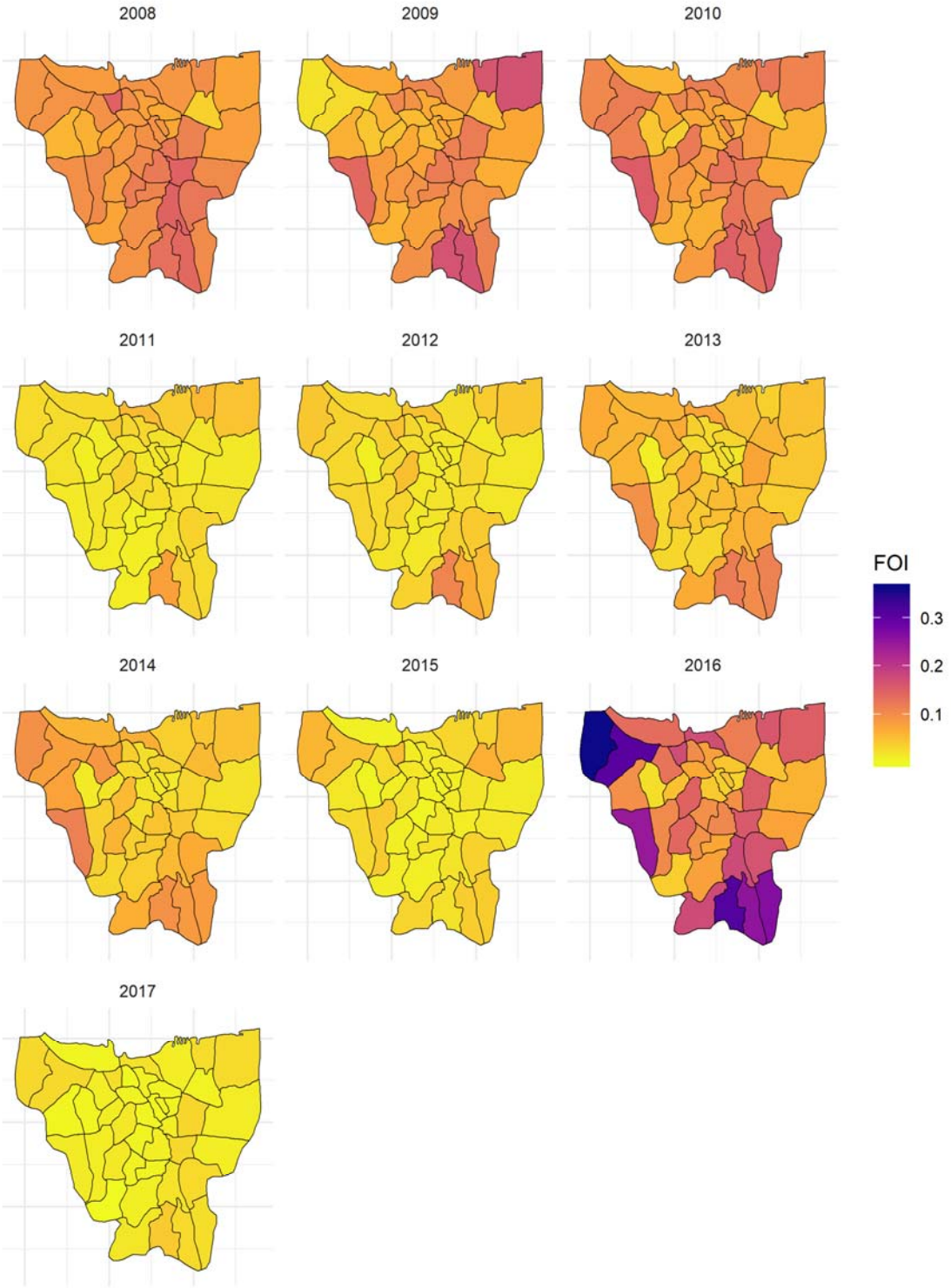
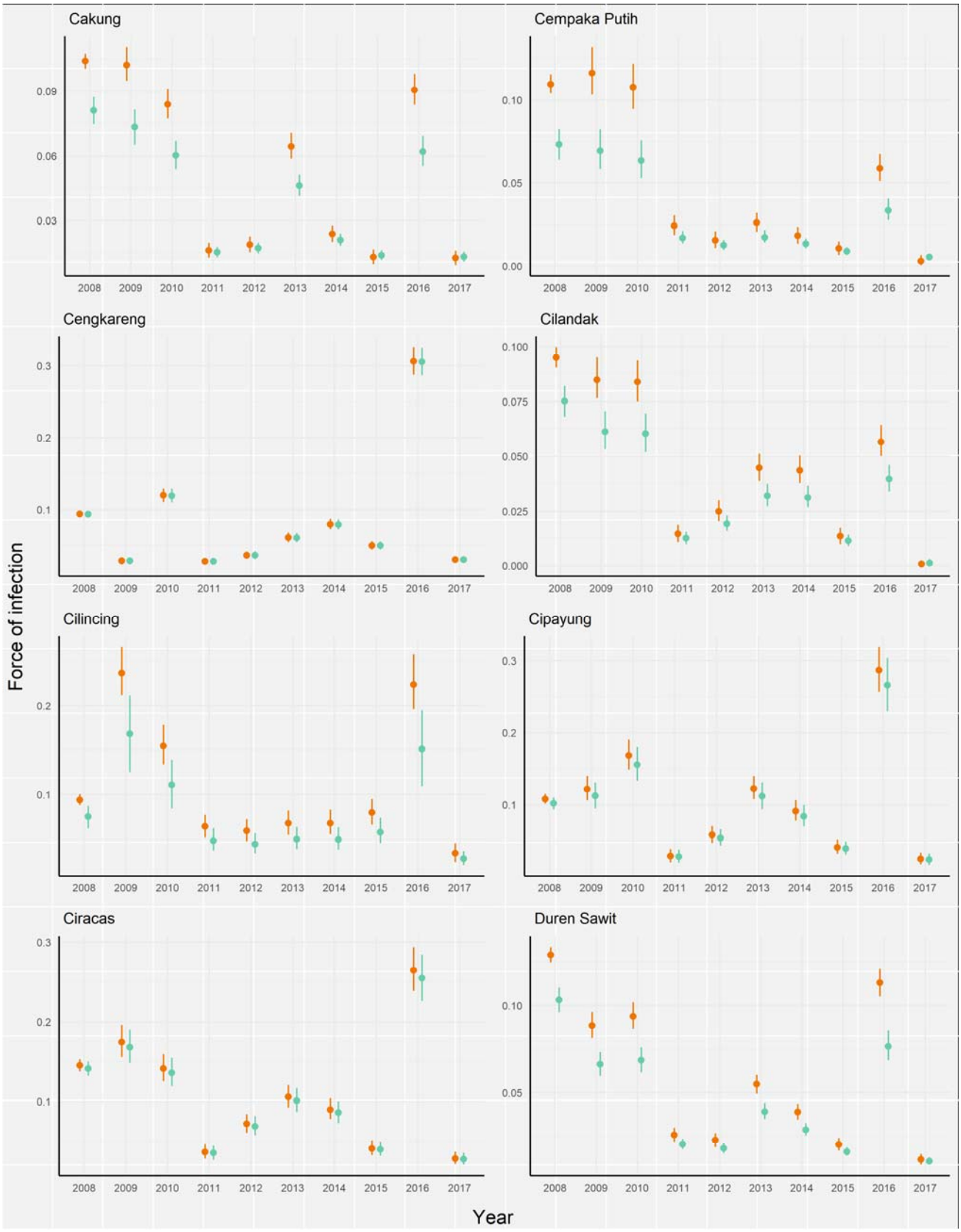
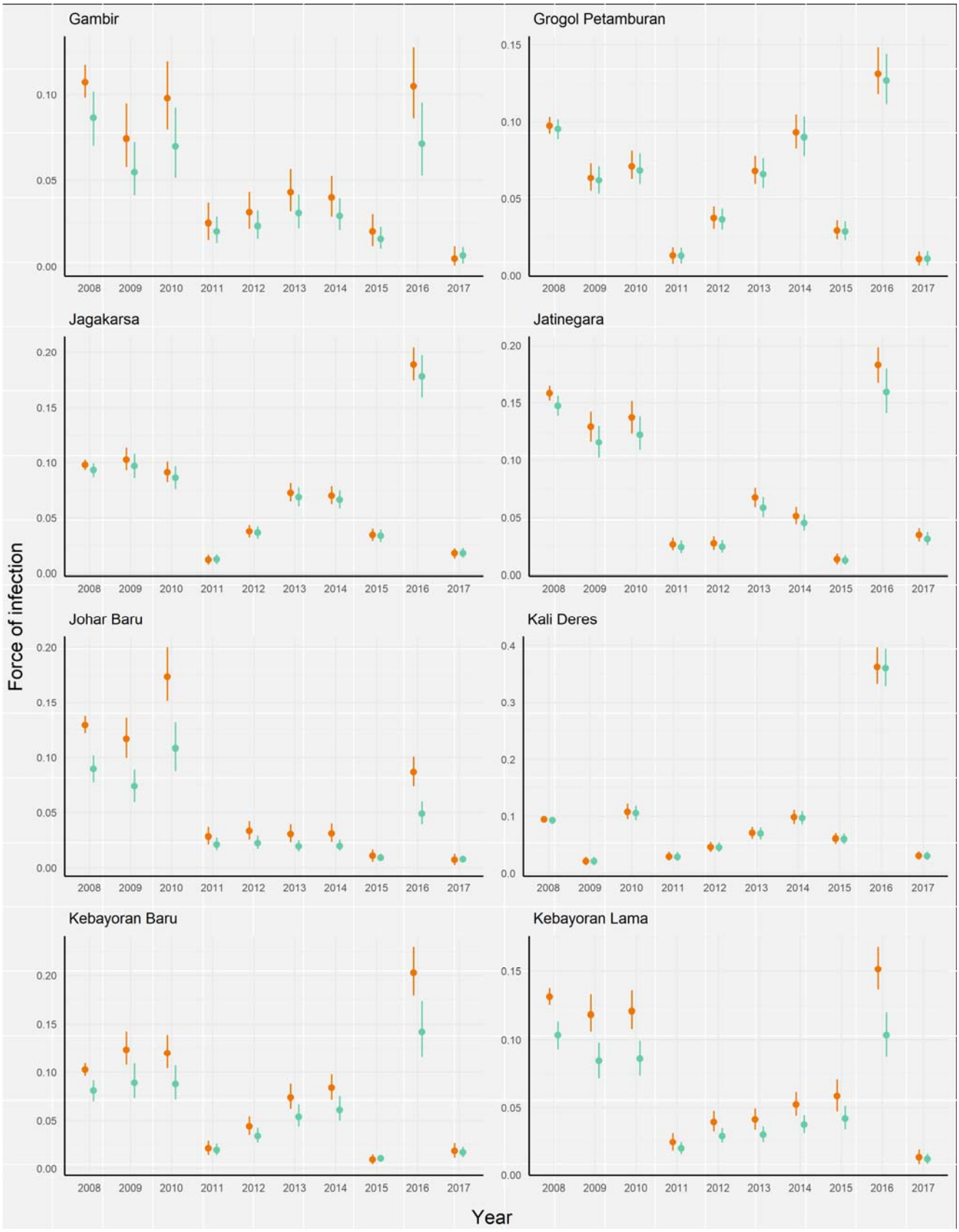
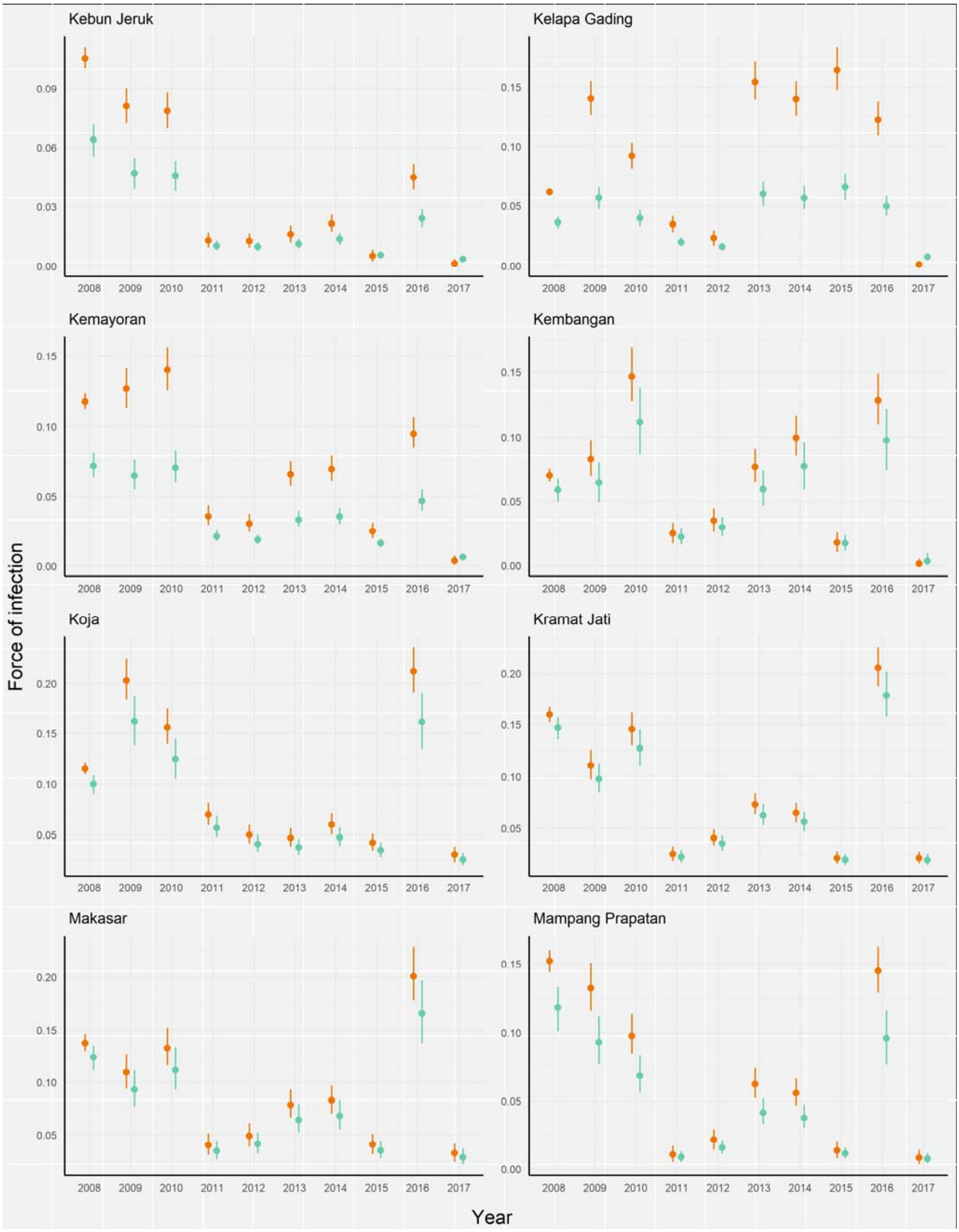
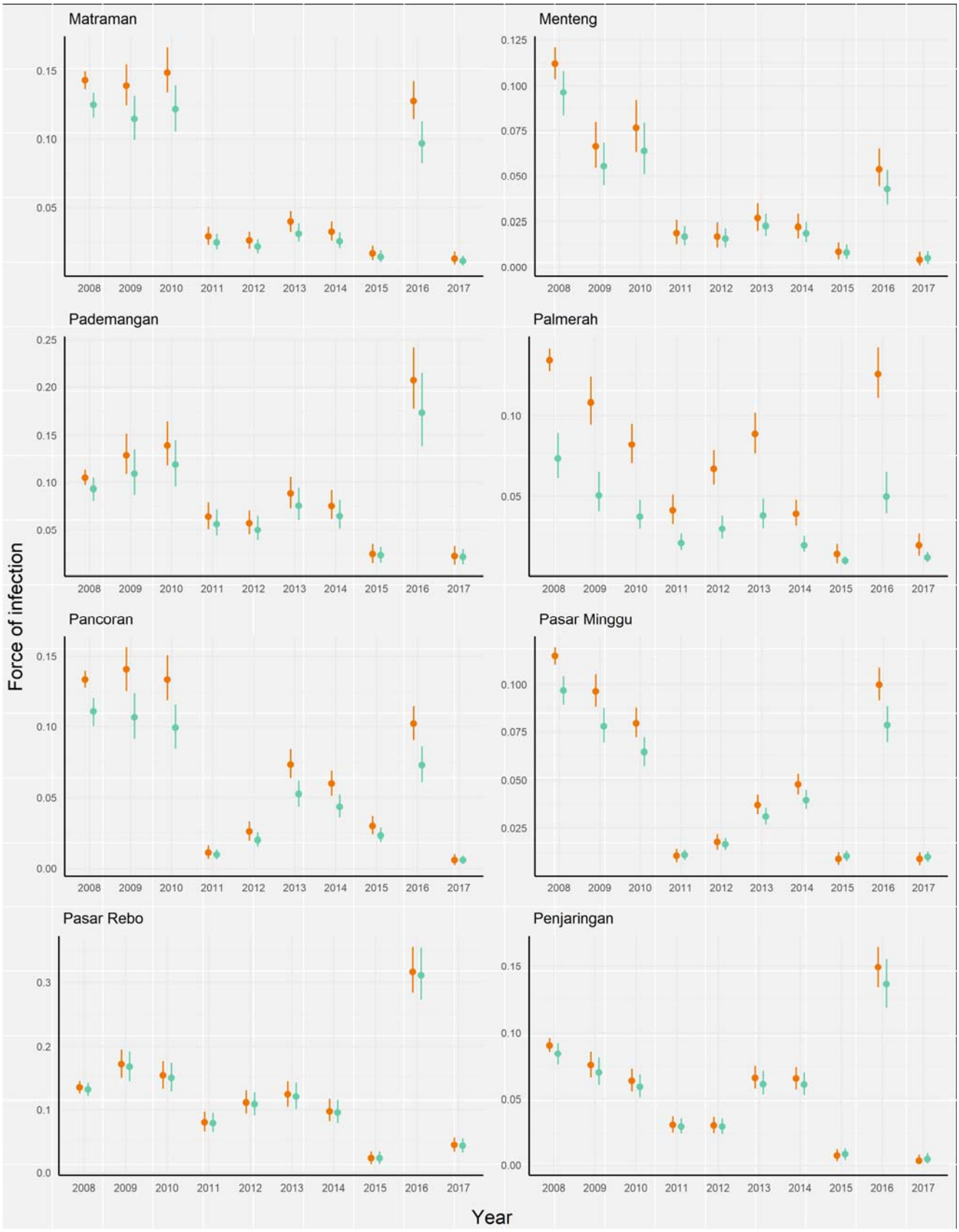


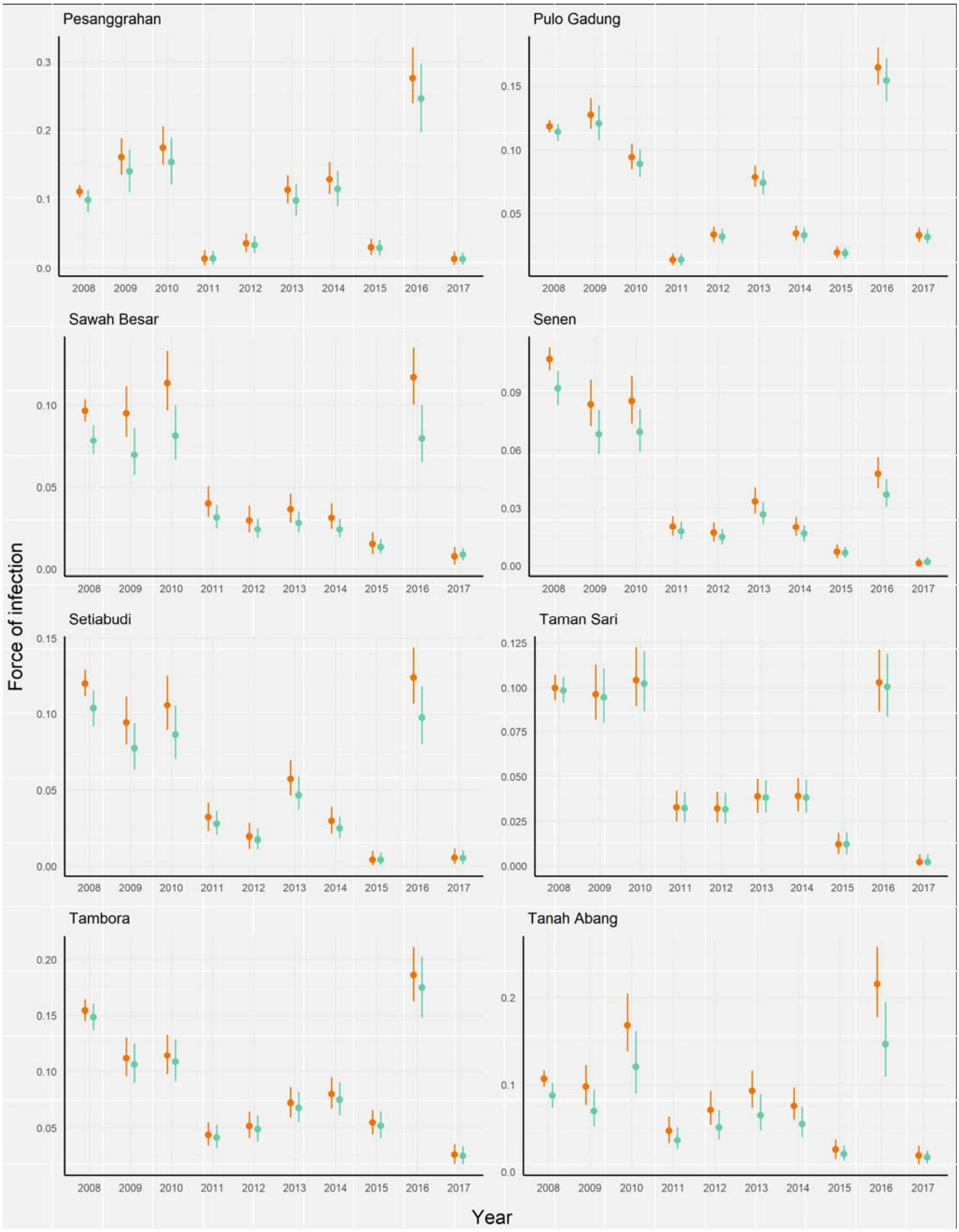
Figure S7. Total transmission intensity (4λ) estimates, median and 95% credible intervals, obtained from the fit of model 2 variants *S* (orange) and *PS* (green) to yearly age-stratified DHF incidence rates reported between 2008 and 2017 in Jakarta's subdistricts. All yearly parameter estimates are available in S3 Supplementary File.




Gambir
Grogol Petamburan
Jagakarsa
Jatinegara
Johar Baru
Kali Deres
Kebayoran Baru
Kebayoran Lama
Force of infection
Year
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017


Kebun Jeruk
Kelapa Gading
Kemayoran
Kembangan
Koja
Kramat Jati
Makasar
Mampang Prapatan
Force of infection
Year
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017


Matraman
Menteng
Pademangan
Palmerah
Pancoran
Pasar Minggu
Pasar Rebo
Penjaringan
Force of infection
Year
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017


Pesanggrahan
Pulo Gadung
Sawah Besar
Senen
Setiabudi
Taman Sari
Tambora
Tanah Abang
Force of infection
Year
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017

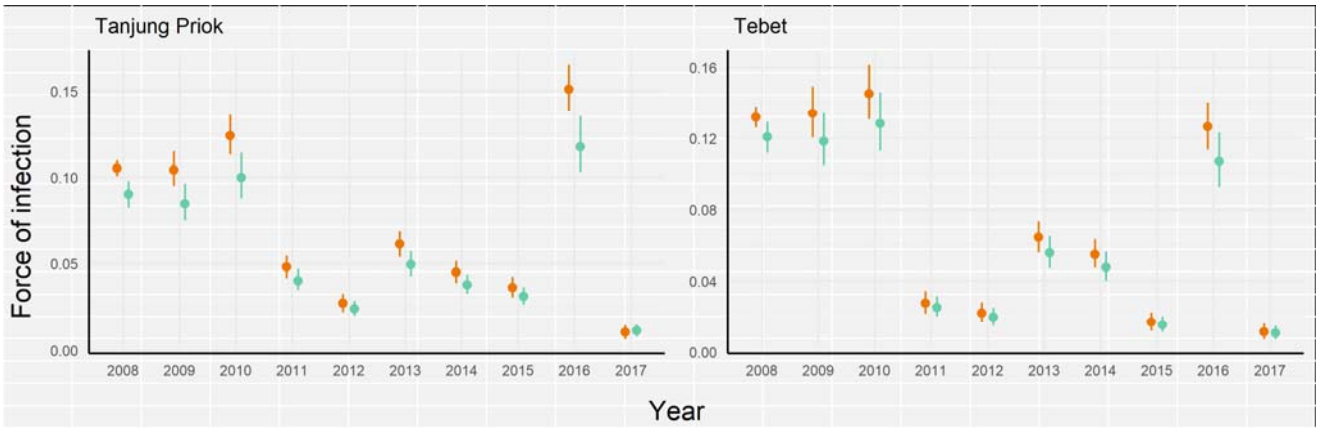
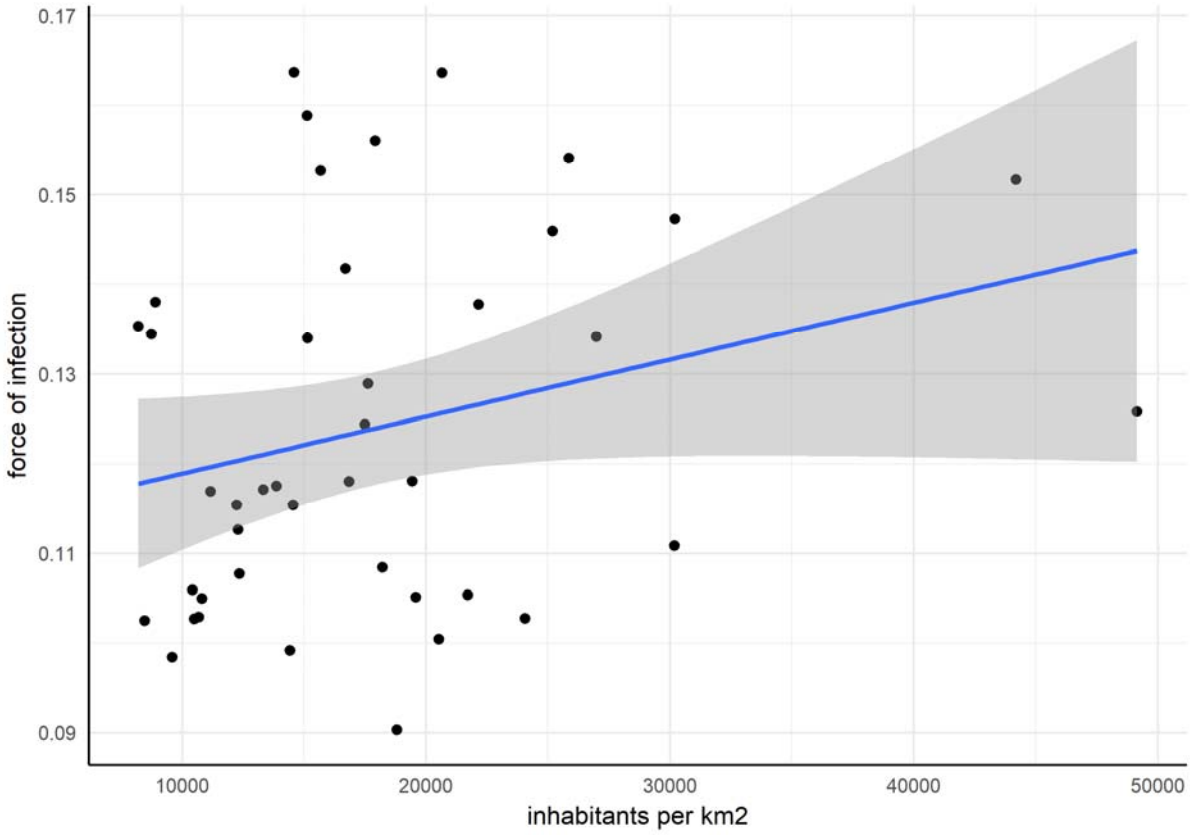
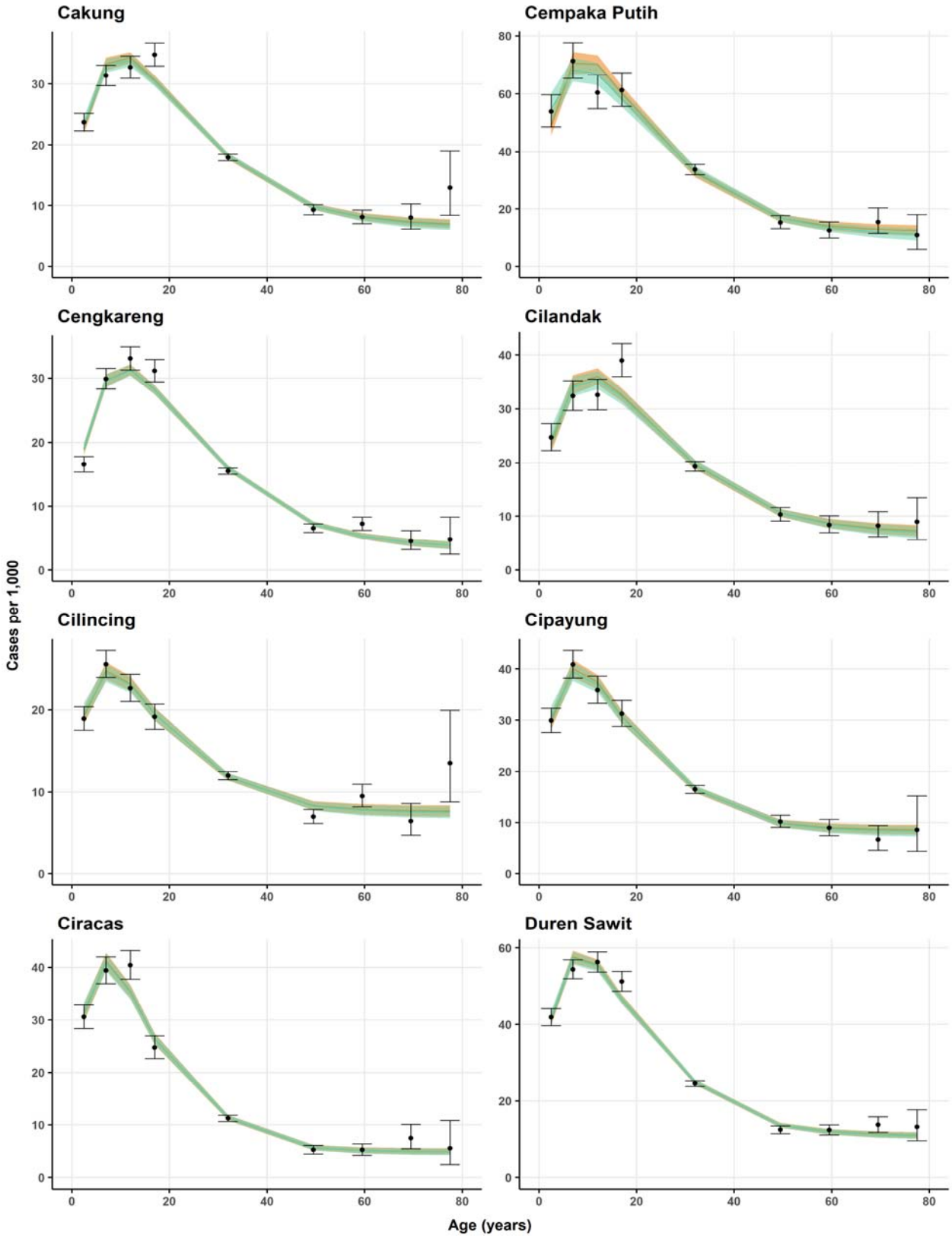


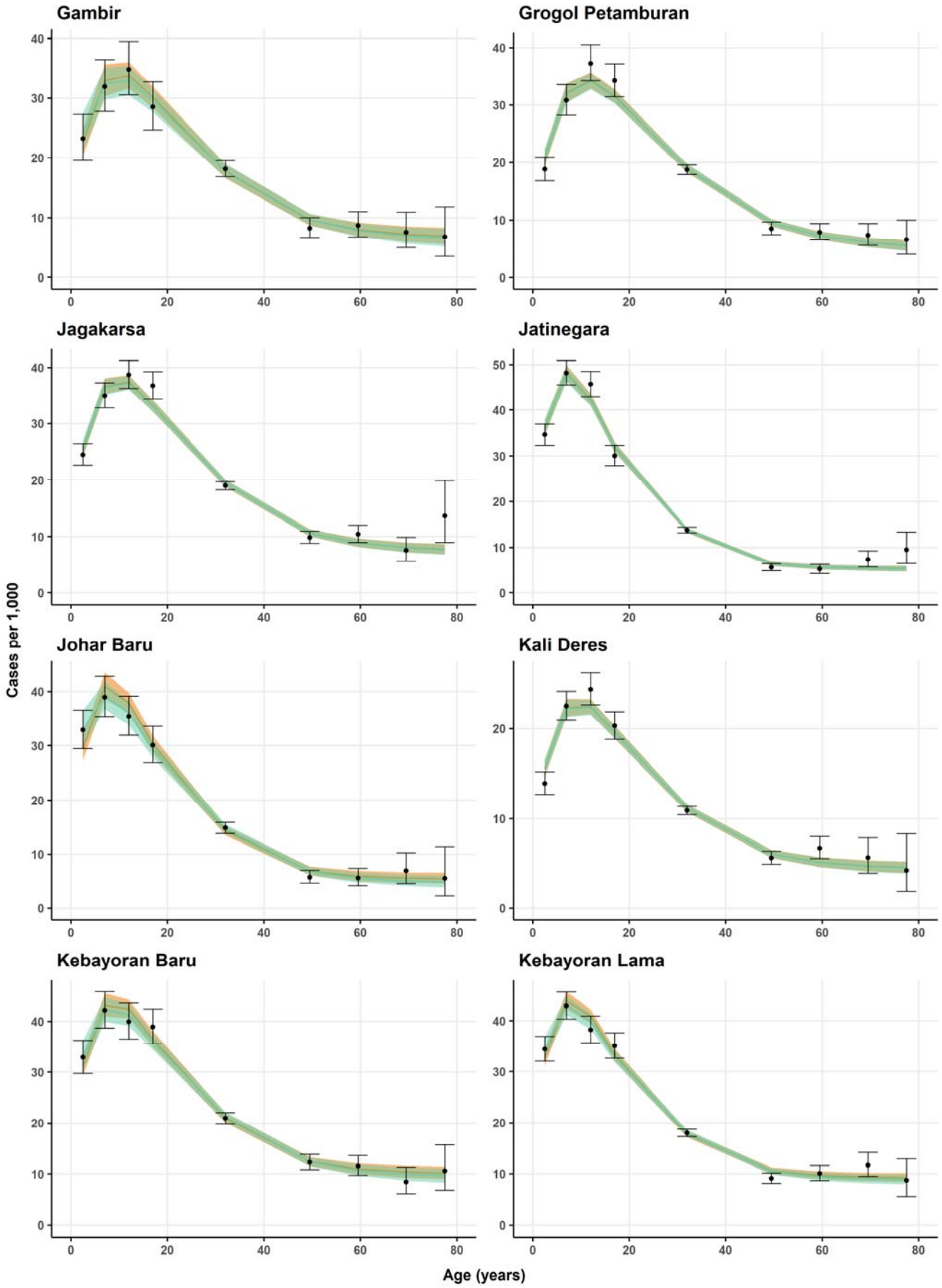
Figure S8. Mean (blue line) and 95% confidence interval (grey shading) of linear regression model between average annual subdistrict total force of infection (4λ) estimates (obtained from the fit of model variant *PS* to average annual age-stratified DHF incidence rates reported in 2008-2017) and subdistrict population density estimates (available online (23)). Adjusted R^2=0.049, P=0.086.

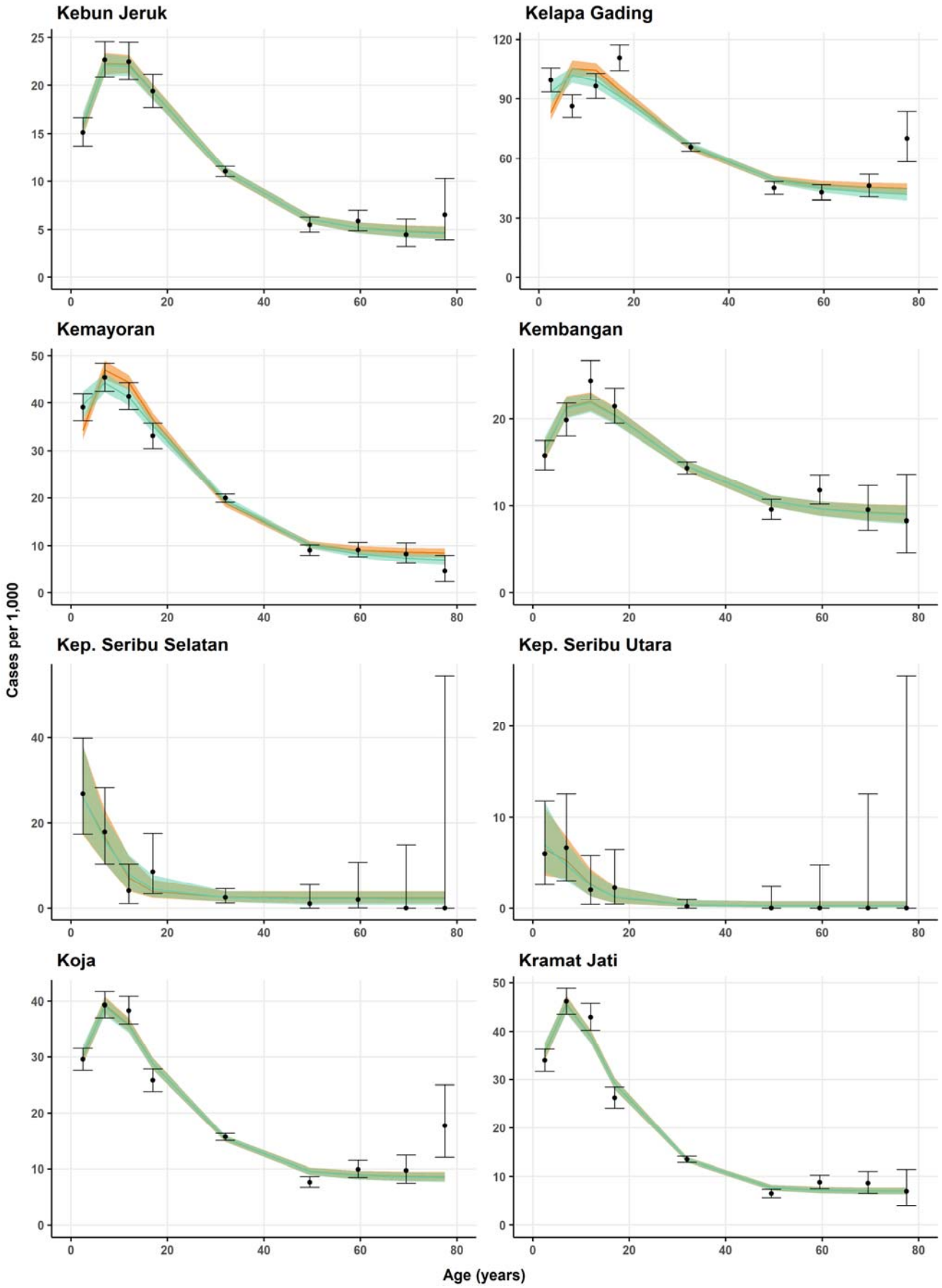


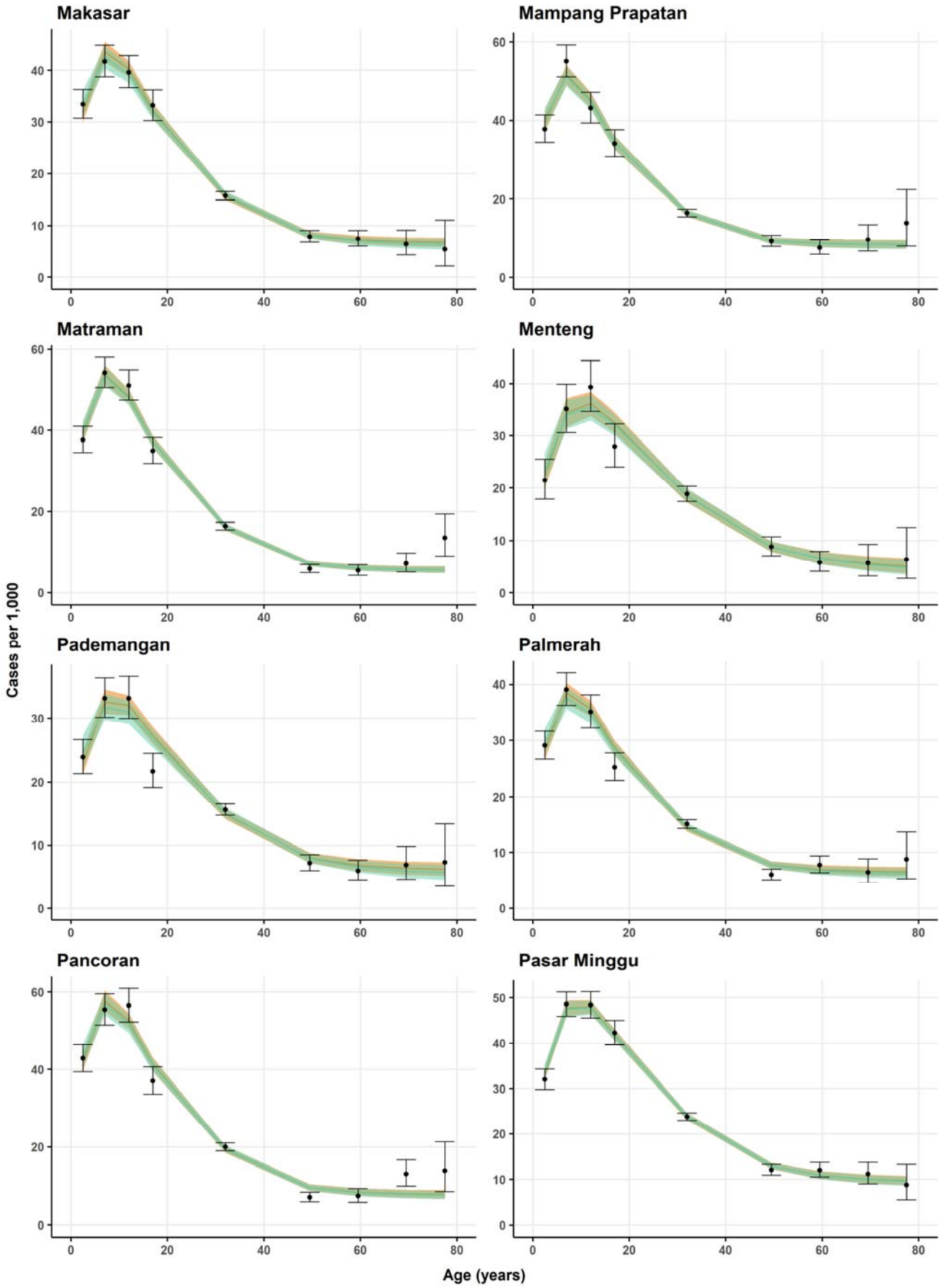
4.3. Jakarta subdistricts: model fits

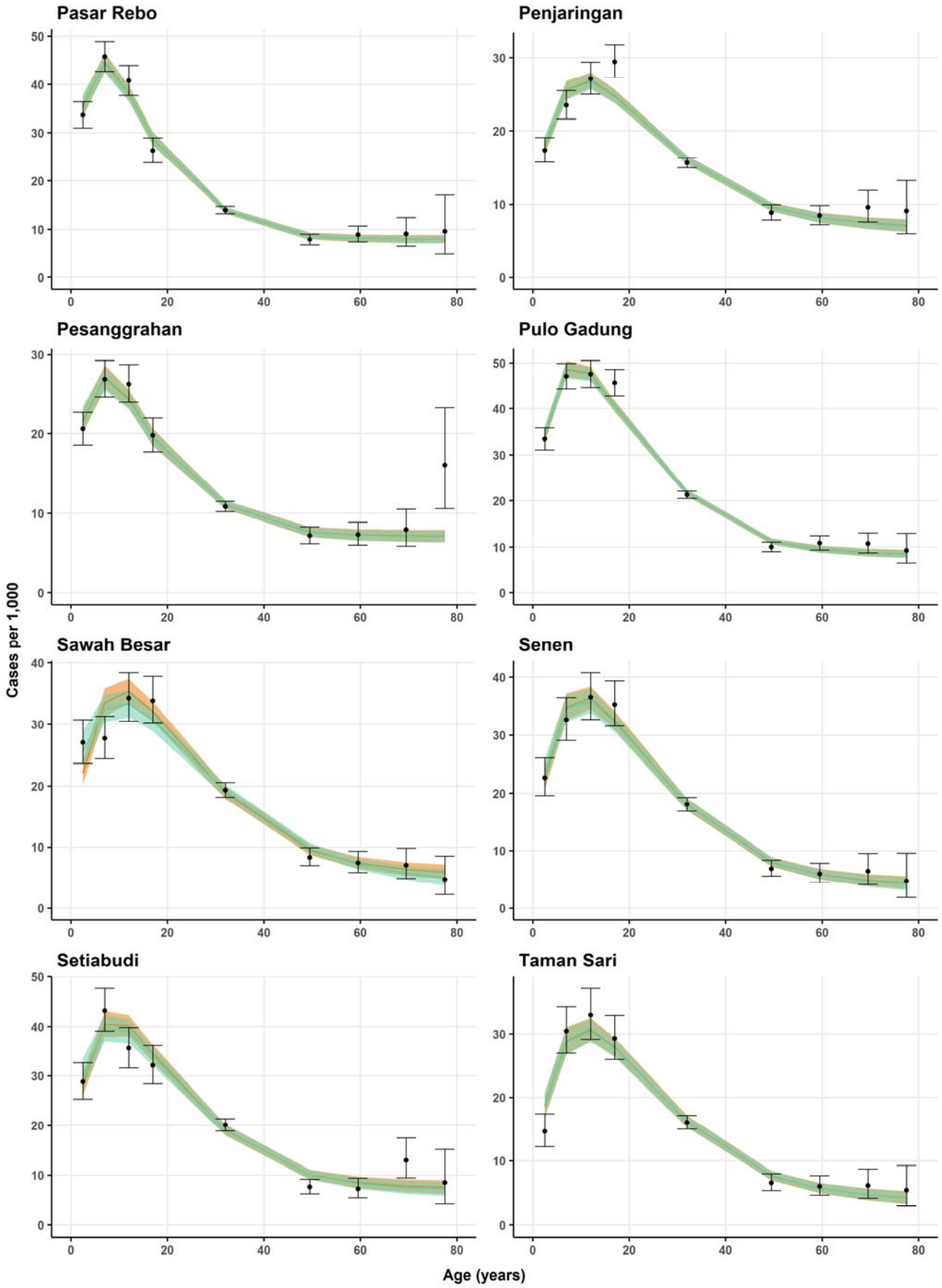
Figure S9. Fit of model 1 variants *S* (orange line and ribbon, indicating median and 95% credible intervals) and *PS* (green line and ribbon, indicating median and 95% credible intervals) to average annual (2008-2017) DHF incidence rates by age (black points and bars, indicating mean and 95% confidence intervals calculated assuming a binomial distribution) reported in Jakarta's subdistricts.




Gambir
Grogol Petamburan
Jagakarsa
Jatinegara
Johar Baru
Kali Deres
Kebayoran Baru
Kebayoran Lama
Cases per 1,000
Age (years)


Kebun Jeruk
Kelapa Gading
Kemayoran
Kembangan
Kep. Seribu Selatan
Kep. Seribu Utara
Koja
Kramat Jati
Cases per 1,000
Age (years)


Makasar
Mampang Prapatan
Matraman
Menteng
Pademangan
Palmerah
Pancoran
Pasar Minggu
Cases per 1,000
Age (years)


Pasar Rebo
Penjaringan
Pesanggrahan
Pulo Gadung
Sawah Besar
Senen
Setiabudi
Taman Sari
Cases per 1,000
Age (years)

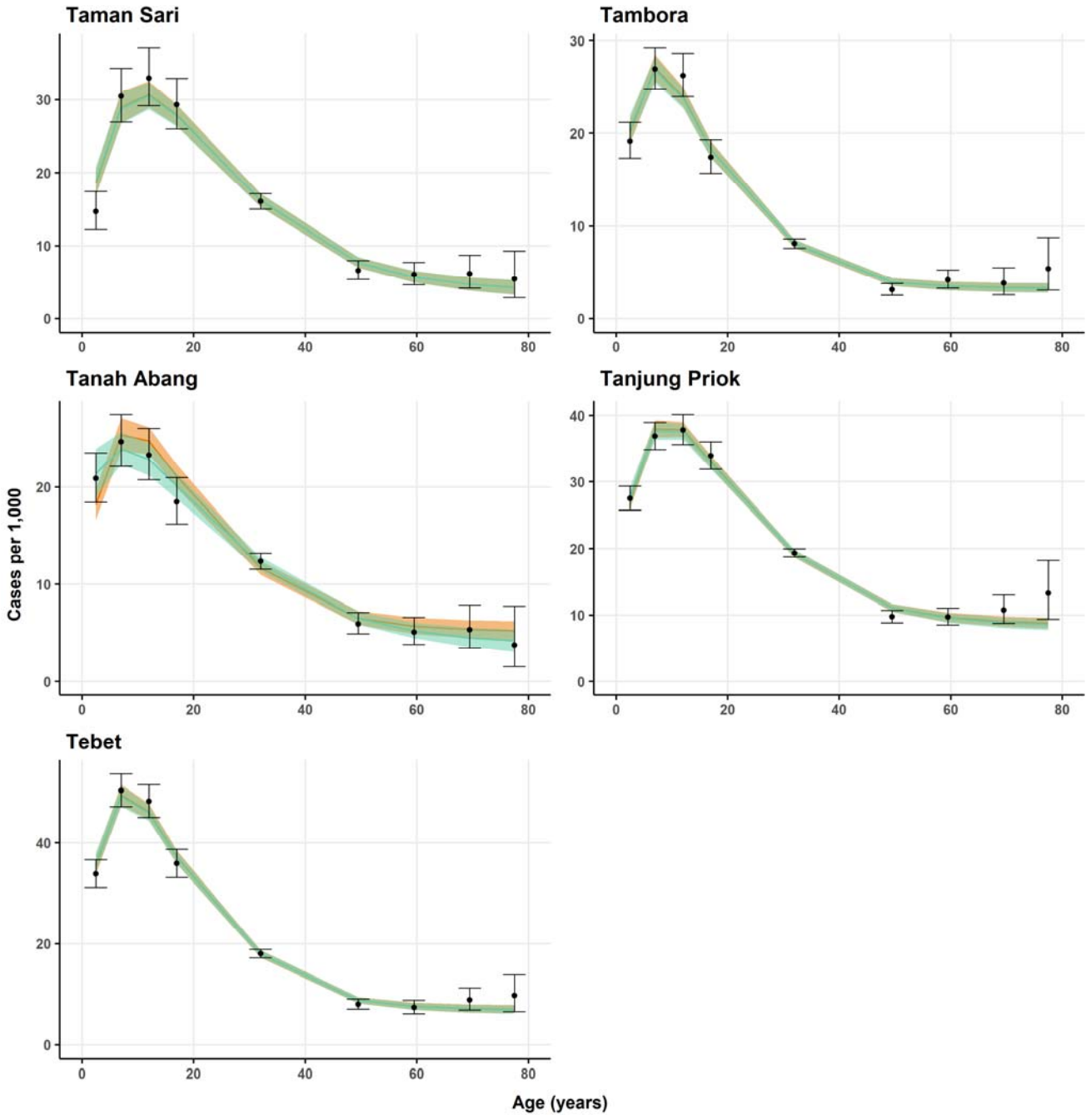
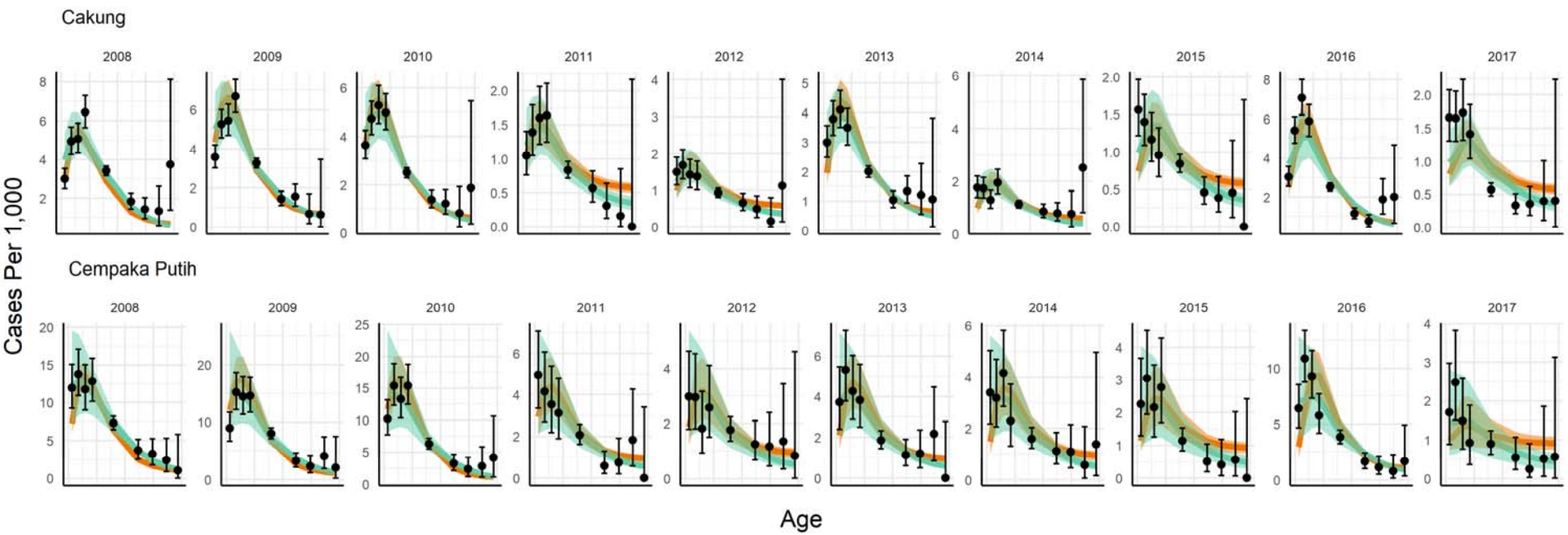
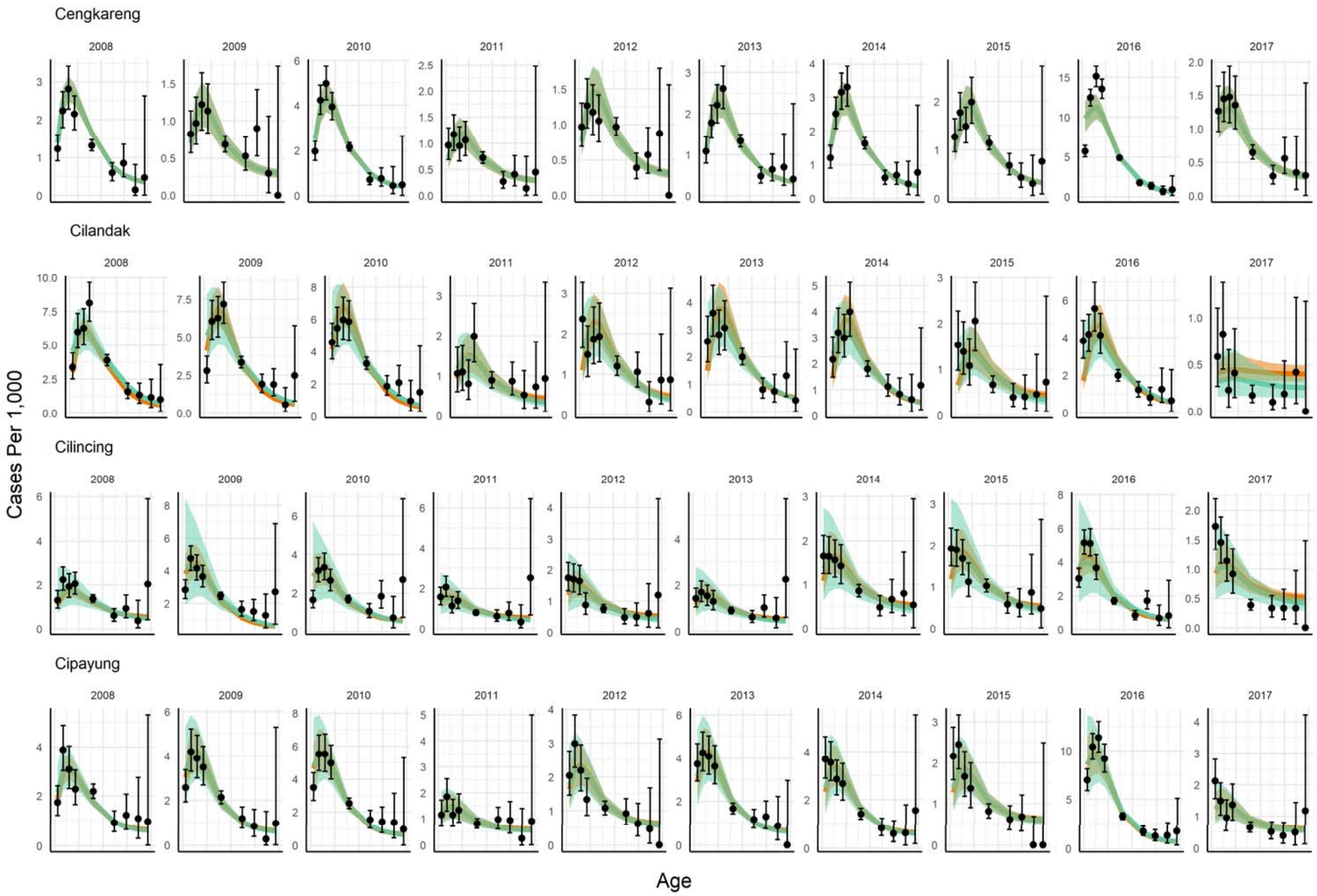
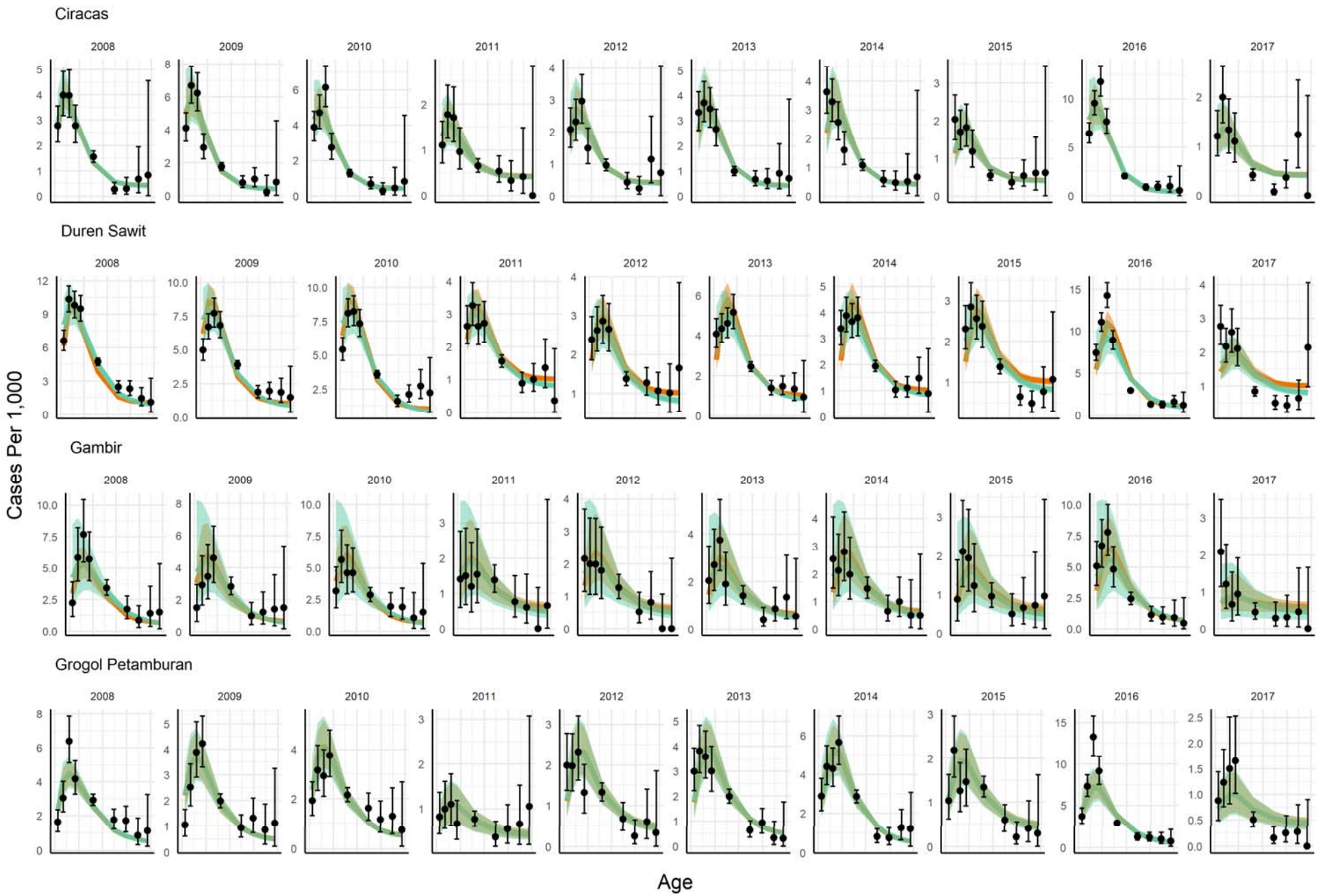
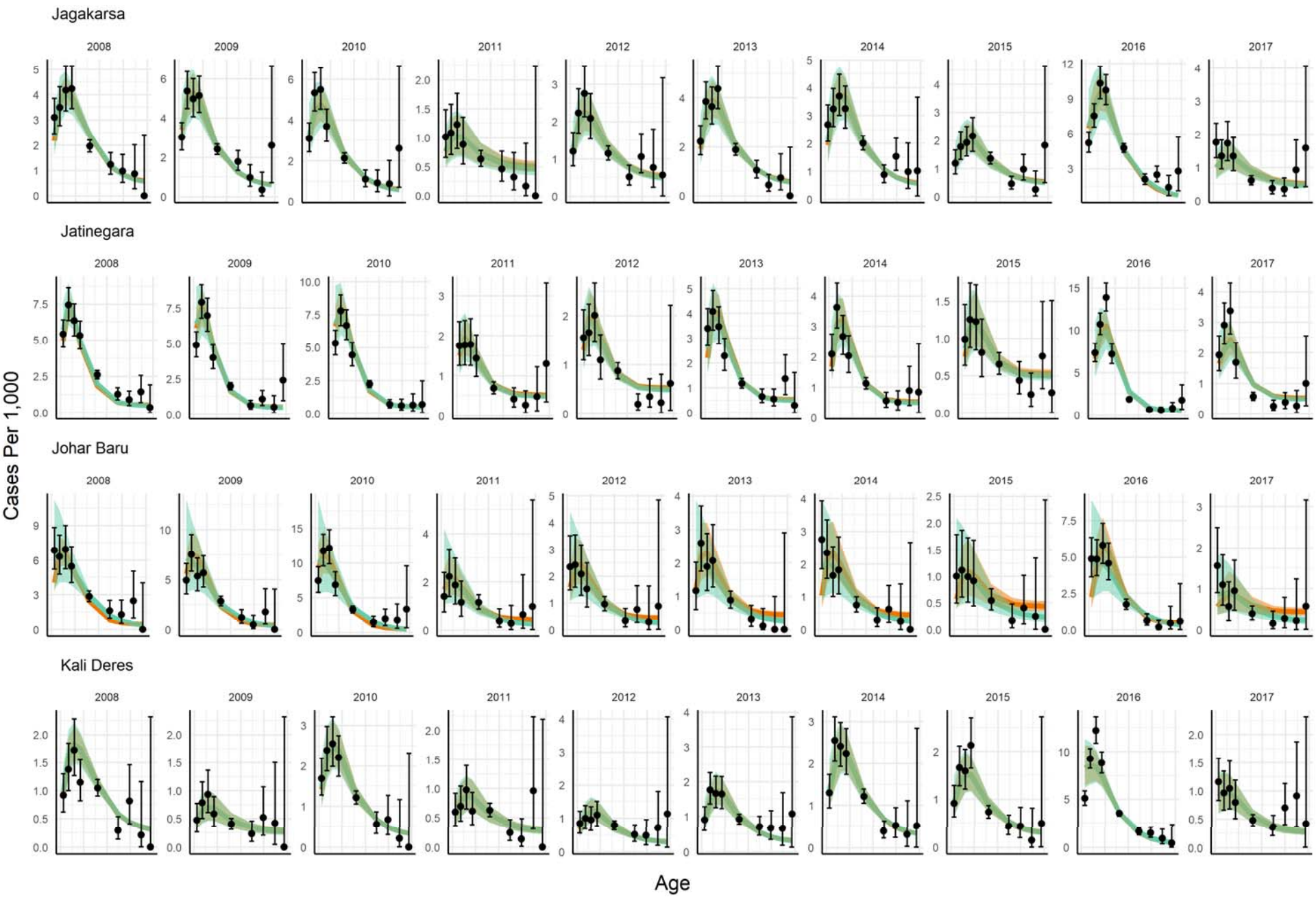

Taman Sari
Tambora
Tanah Abang
Tanjung Priok
Tebet
Cases per 1,000
Age (years)

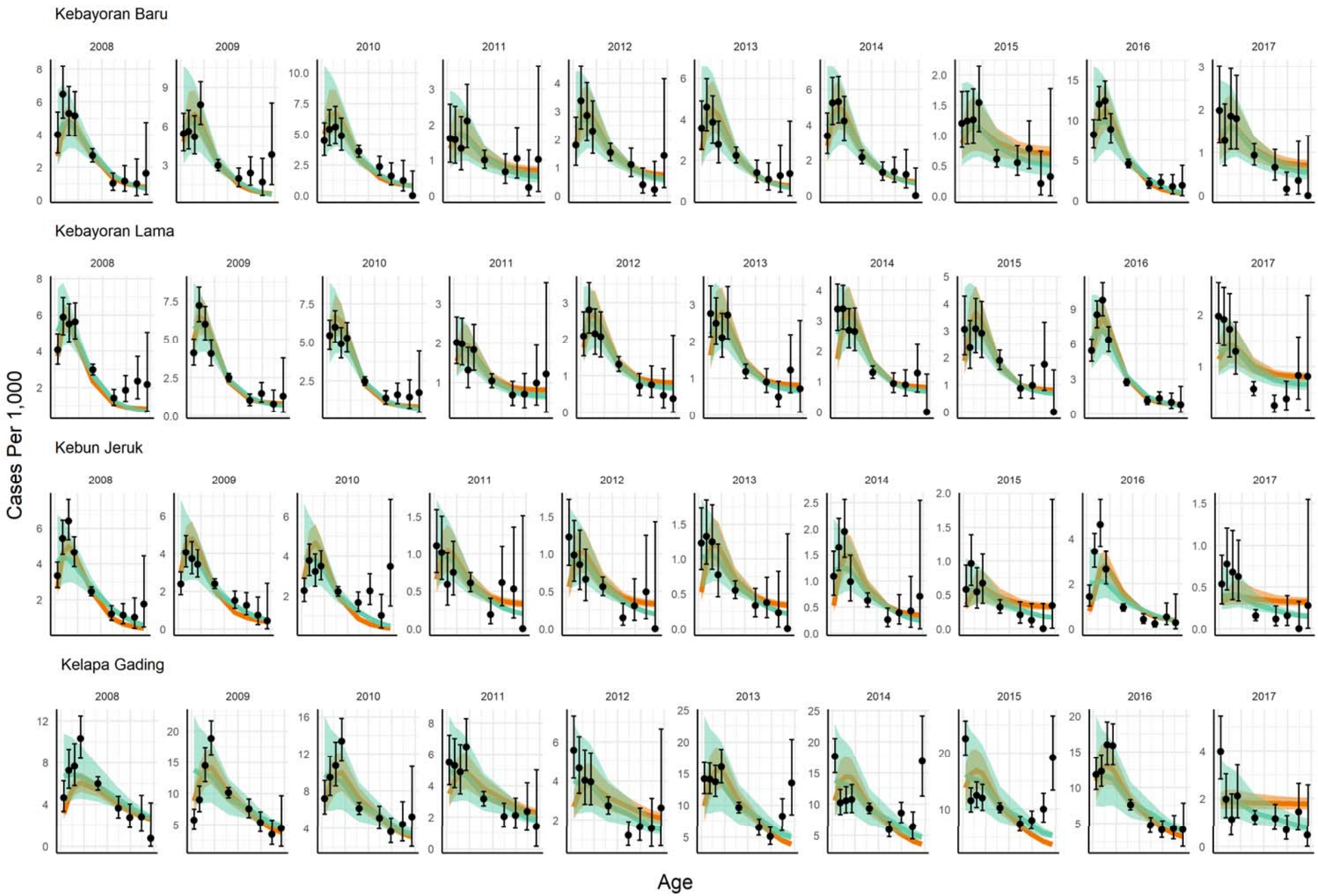
Figure S10. Fit of model 2 variants *S* (orange line and ribbon, indicating median and 95% credible intervals) and *PS* (green line and ribbon, indicating median and 95% credible intervals) to yearly (2008-2017) DHF incidence rates by age (black points and bars, indicating mean and 95% confidence intervals calculated assuming a binomial distribution) reported in Jakarta's subdistricts.

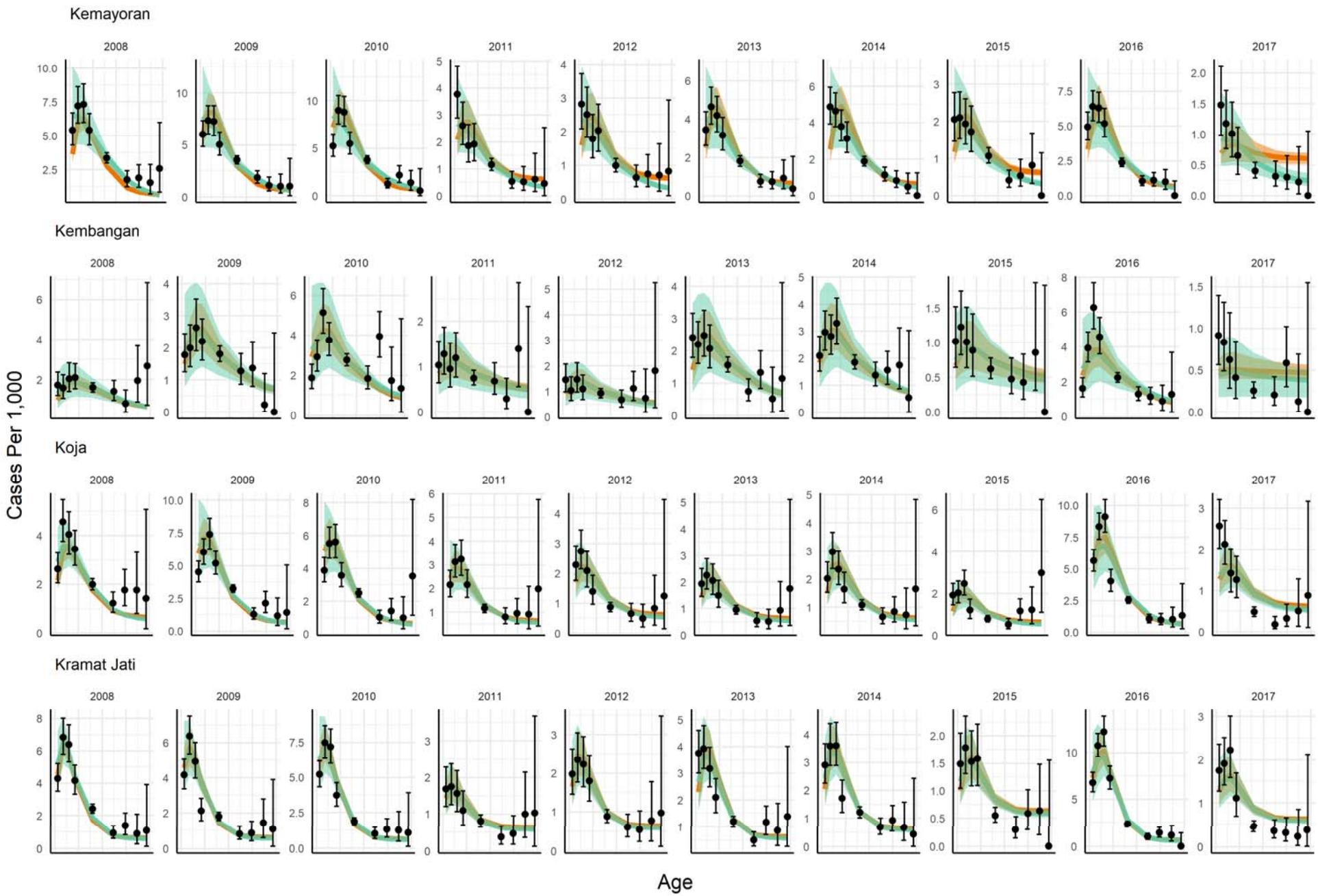


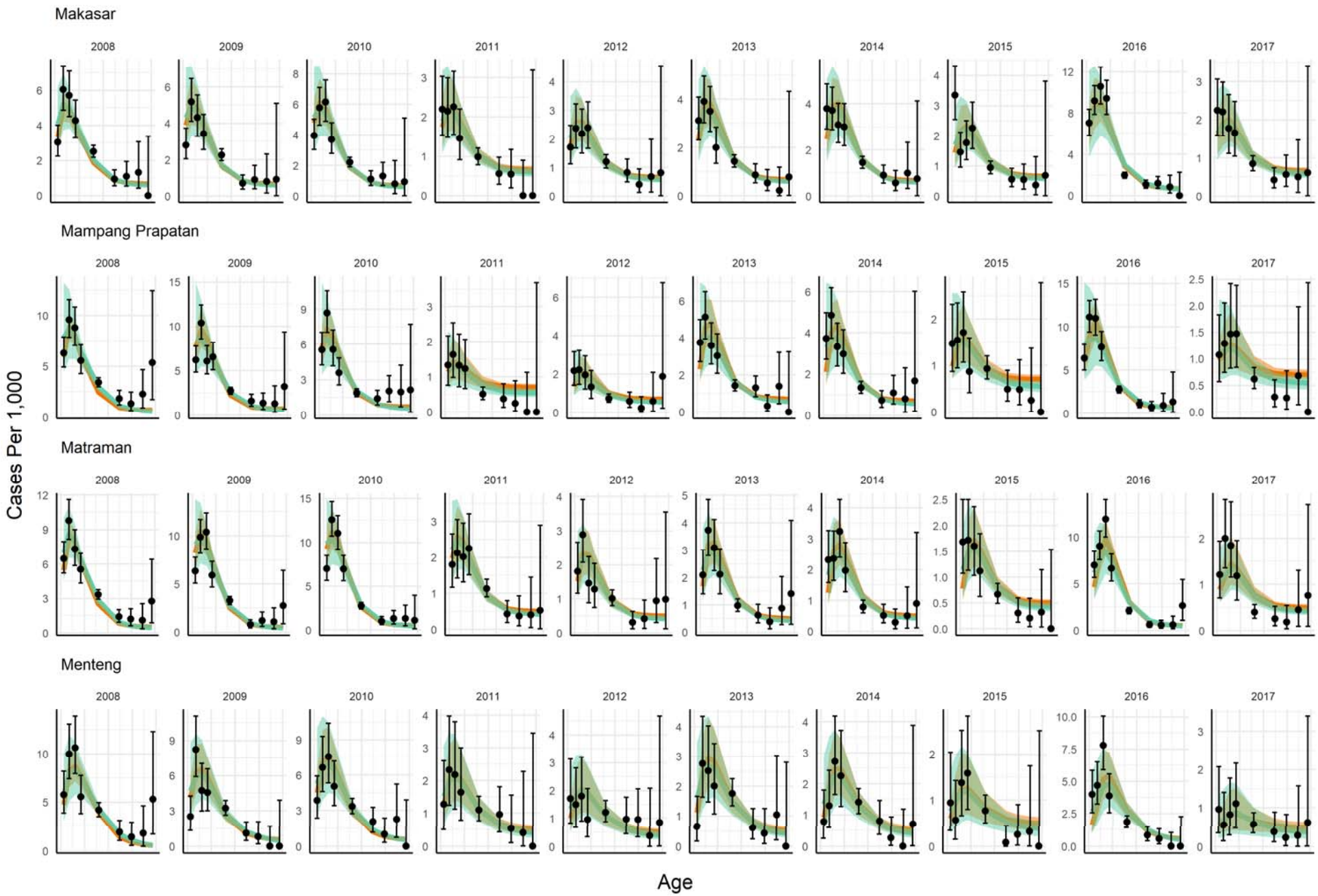

Cengkareng
Cilandak
Cilincing
Cipayung
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Cases Per 1,000
Age

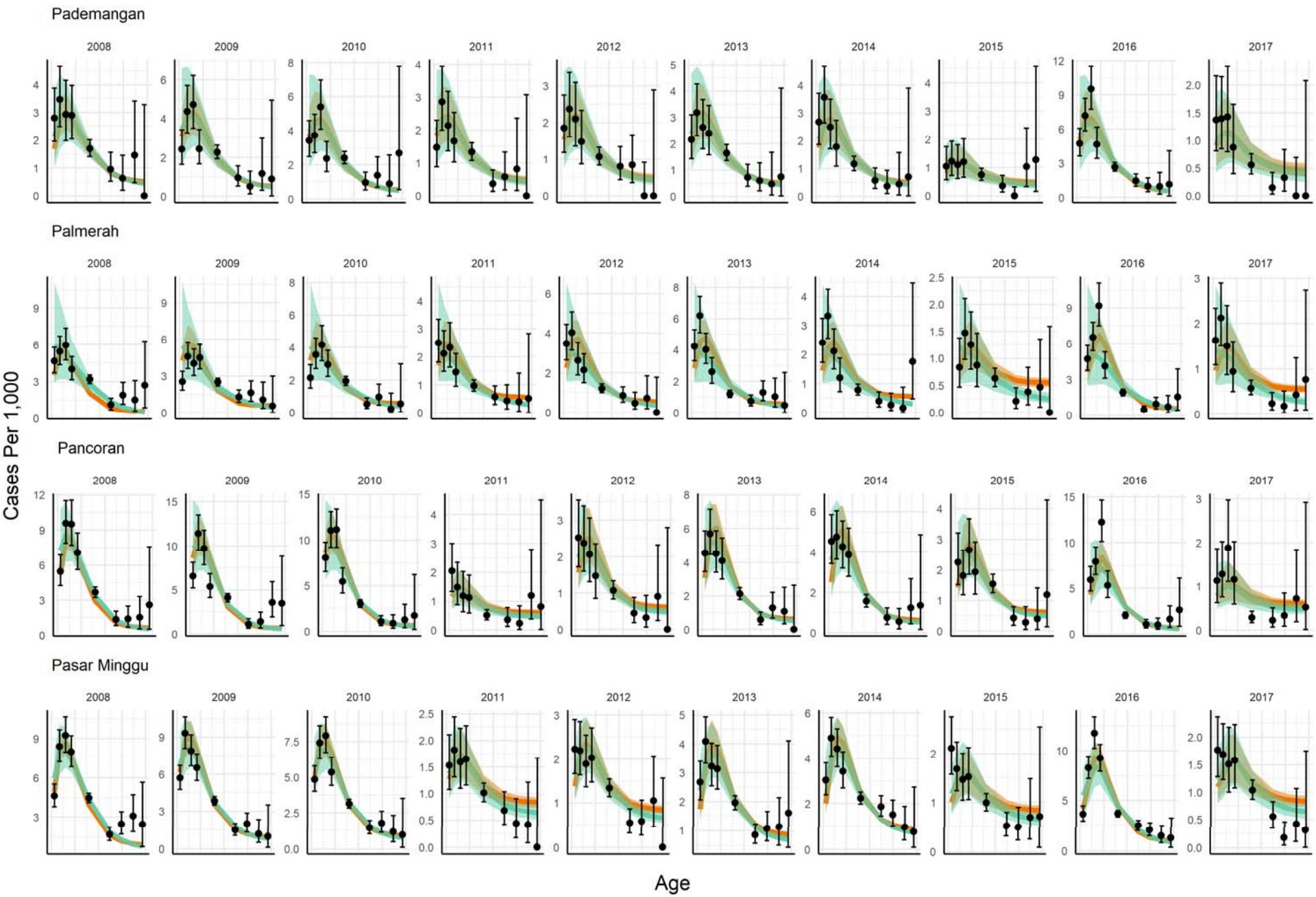

Ciracas
Duren Sawit
Gambir
Grogol Petamburan
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Cases Per 1,000
Age

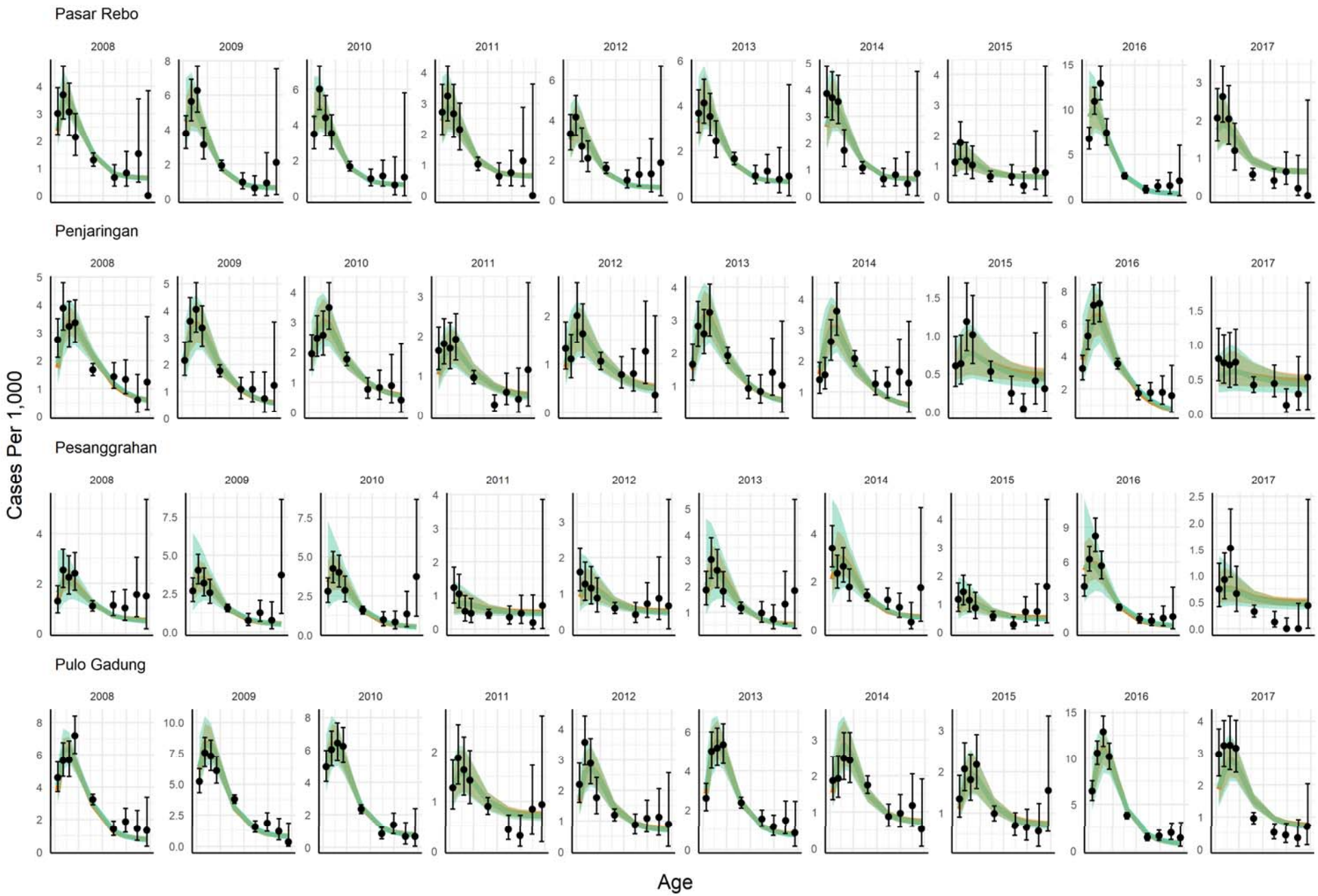

Jagakarsa
Jatinegara
Johar Baru
Kali Deres
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Cases Per 1,000
Age

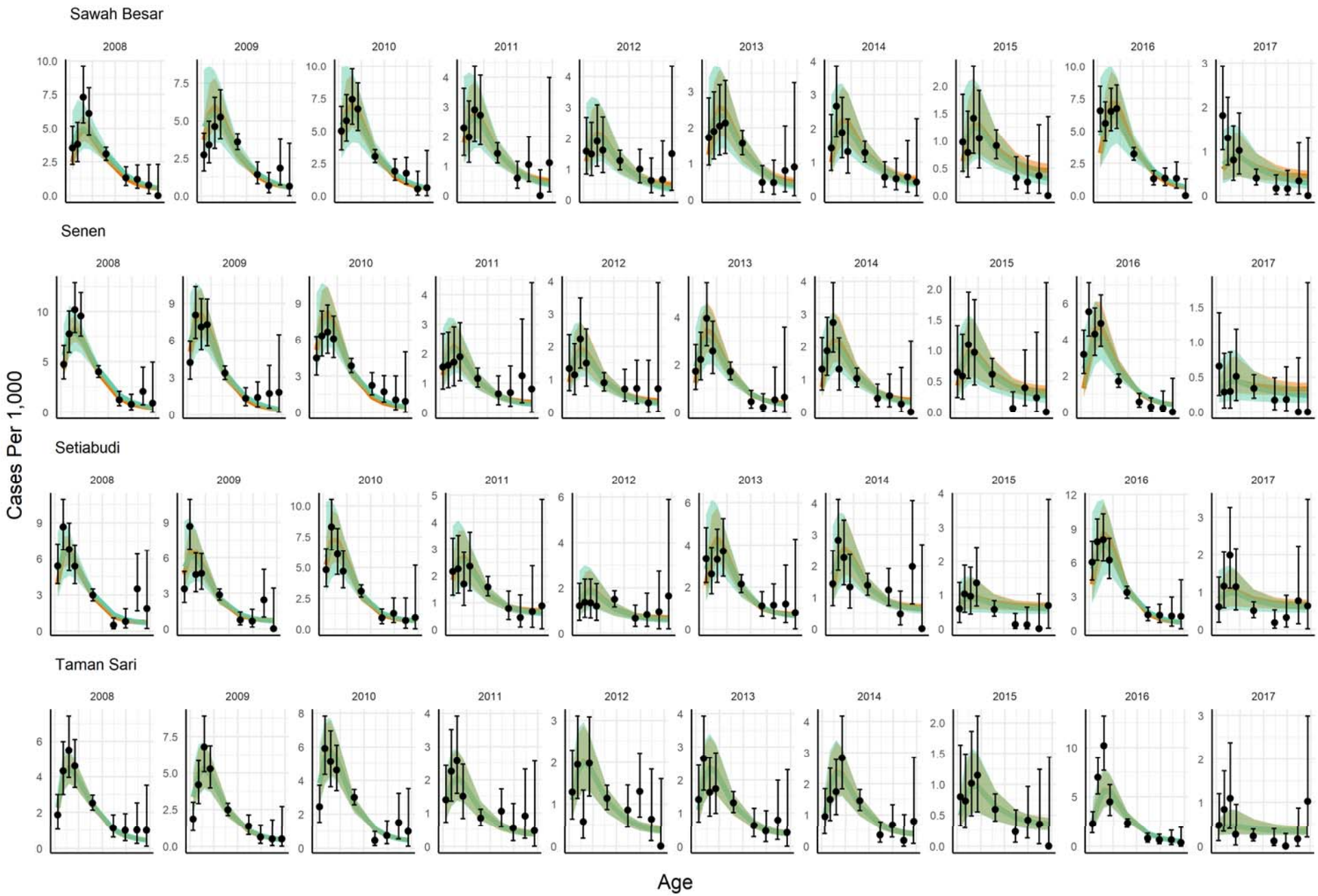

Kebayoran Baru
Kebayoran Lama
Kebun Jeruk
Kelapa Gading
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Cases Per 1,000
Age

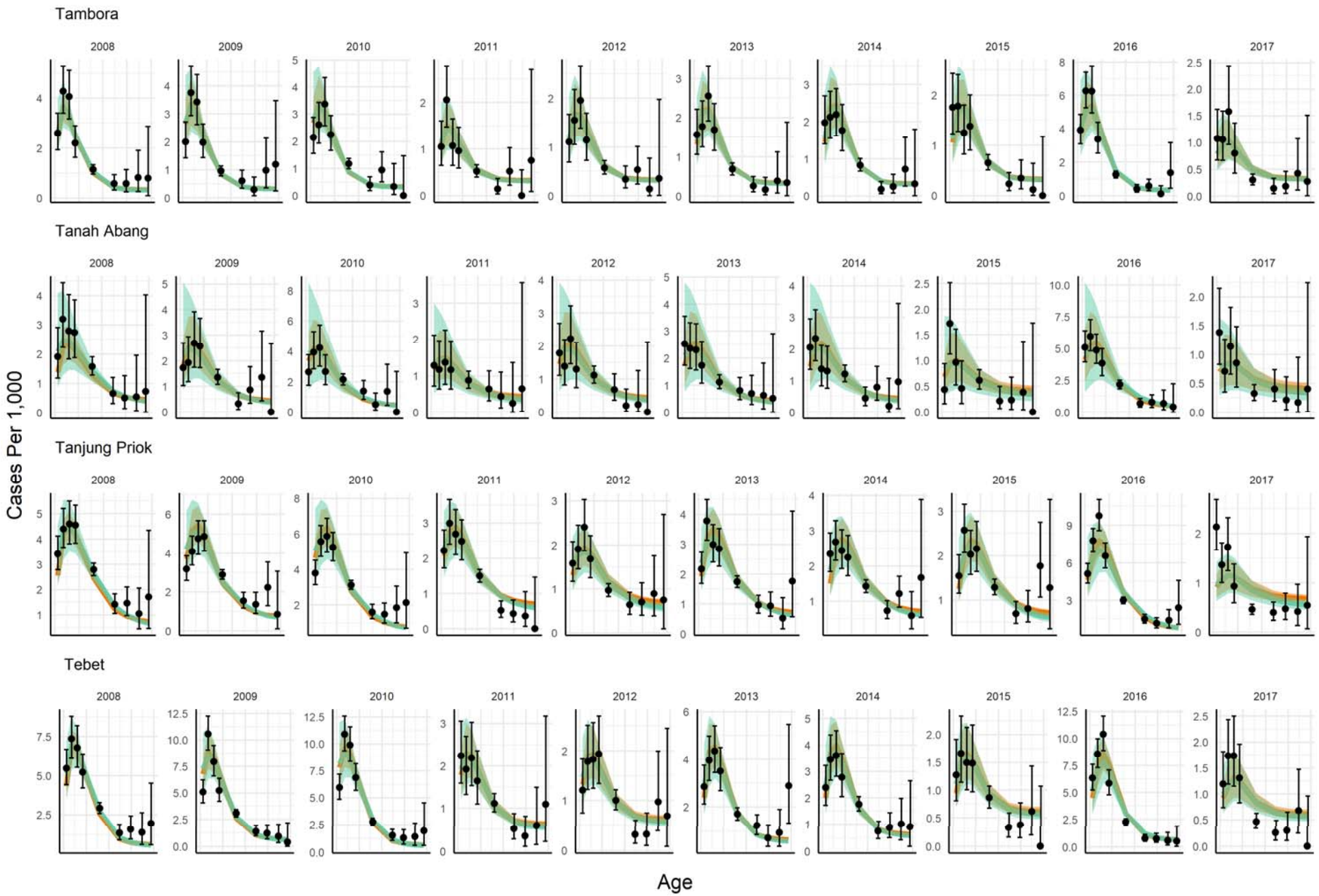

Kemayoran
Kembangan
Koja
Kramat Jati
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Cases Per 1,000
Age


Makasar
Mampang Prapatan
Matraman
Menteng
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Cases Per 1,000
Age


Pademangan
Palmerah
Pancoran
Pasar Minggu
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Cases Per 1,000
Age


Pasar Rebo
Penjaringan
Pesanggrahan
Pulo Gadung
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Cases Per 1,000
Age


Sawah Besar
Senen
Setiabudi
Taman Sari
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Cases Per 1,000
Age


Tambora
Tanah Abang
Tanjung Priok
Tebet
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Cases Per 1,000
Age