Assessing dengue control in Tokyo, 2014

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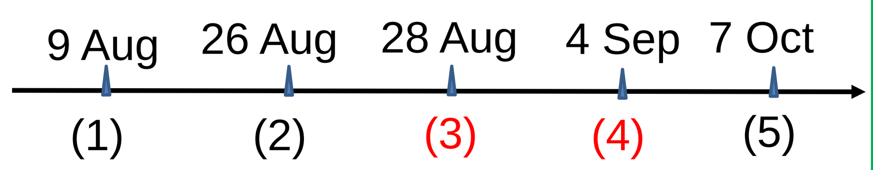
Introduction

In summer 2014, an autochthonous outbreak of dengue occurred in Tokyo, in which Yoyogi Park acted as the focal area of transmission[1]. Recognizing the outbreak, concerted efforts were made to control viral spread, which included mosquito control, public announcement of the outbreak, and a total ban on entering the park.



(1) Illness onset in the index case
(2) Confirmed diagnosis of the index case
(3) Interventions against mosquitos with public dissemination of the outbreak
(4) Closure of Yoyogi Park
(5) Illness onset in the last case

Purpose: (1) estimate the generation time and the effective reproduction number;
(2) assess the effectiveness of control measures.

Data

The reported cases were classified into:
(i) Group 1: complete observation;
(ii) Group 2: interval-censored observation;
(iii) Group 3: missing observation of exposure.

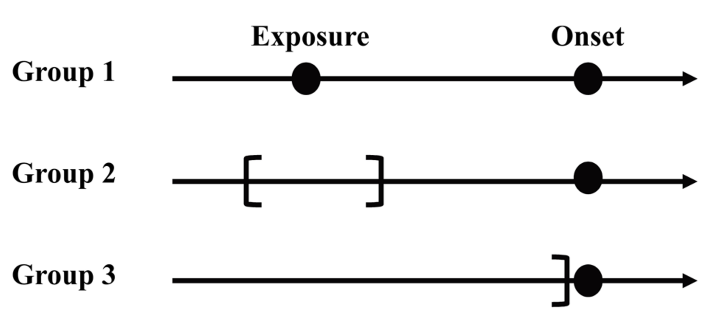


Fig 1. Illustrated time of exposure and classification of cases

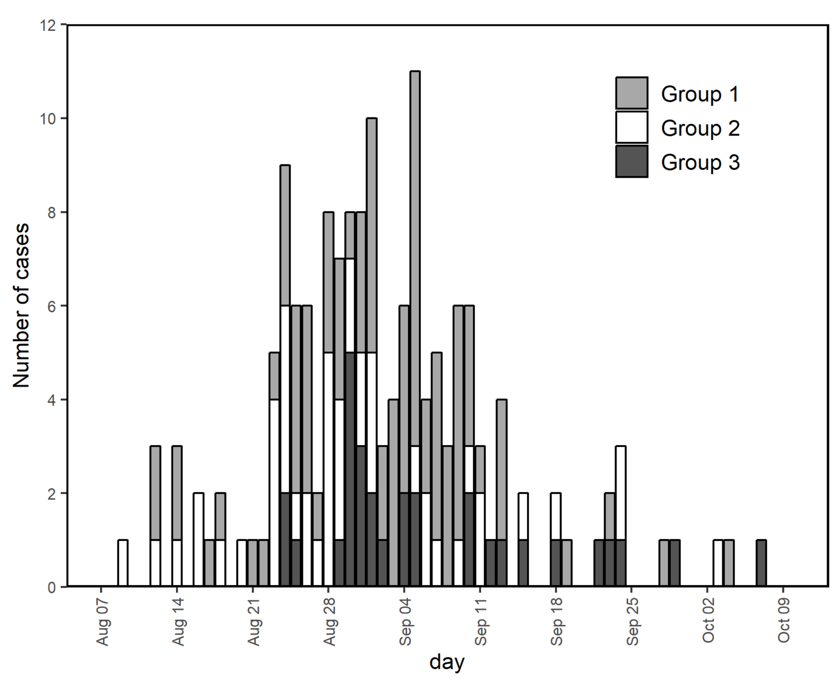


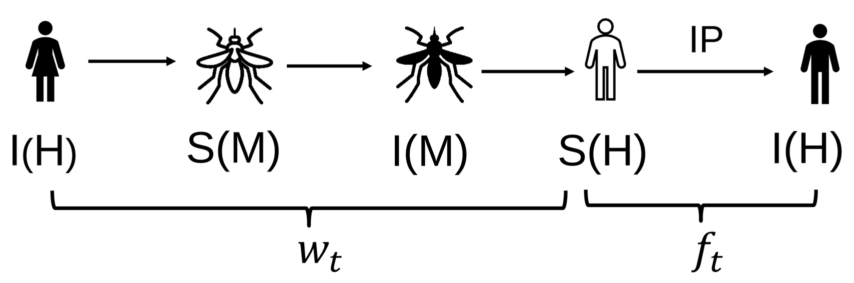
Fig 2. Temporal distribution of dengue by three classification groups of datasets

Group 1: 79; Group 2: 47; Group 3: 30

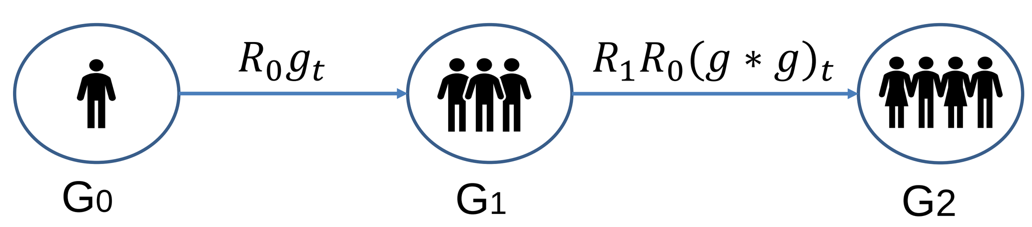
Model

Epidemic curve as the probabiltiy distribution

- Generation time: $g_t = \sum_{\tau=0}^{t} f_{t-\tau} w_\tau$.



- Generation-dependent model[2]



The epidemic curve of infection as the probability distribution **without interventions** (up to the fourth generation (G4)):

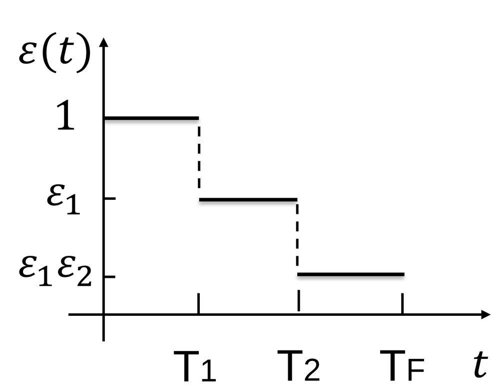
$$h(t) = \frac{g_t + R_1(g*g)_t + R_2R_1(g*g*g)_t + R_3R_2R_1(g*g*g*g)_t}{1 + R_1 + R_2R_1 + R_3R_2R_1}$$

where R_n is the reproduction number of n+1 generation infections.

Effectiveness of interventions

The relative reduction in reproduction number, $\varepsilon(t)$:

$$\varepsilon(t) = \begin{cases} 1 & t < T_1 \\ \varepsilon_1 & T_1 \le t < T_2 \\ \varepsilon_1\varepsilon_2 & T_2 \le t \end{cases}$$



T1: the time when mosquito control was taken

T2: the time when Yoyogi Park was closed

- The probability density of the epidemic curve of infection **with interventions**

$$u(t) = \frac{h(t)\varepsilon(t)}{\sum_{\tau=0}^{T} h(\tau)\varepsilon(\tau)}$$

- The effective reproductive number $R(t) = \frac{u_t}{\sum_{\tau=0}^{t} u_{t-\tau} g_\tau}$

Likelihood function

Group 1, $L_i^1(\Theta_n; t_i^e, t_i^s, d_0) = u_{z(t_i^e, d_0)} f_{t_i^s - t_i^e}$

Group 2, $L_j^2(\Theta_n; E_j^L, E_j^R, t_j^s, d_0) = \sum_{\tau=E_j^L}^{E_j^R} u_{z(\tau, d_0)} f_{t_j^s - \tau}$

Group 3, $L_k^3(\Theta_n; t_k^s, d_0) = \sum_{\tau=t_0}^{t_k^s} u_{z(\tau, d_0)} f_{t_k^s - \tau}$

Incubation period,

$$L^{IP}(\mu_{IP}, \sigma_{IP}; t^e, t^s) = \prod_{i=1}^{n_1} f_{t_i^s - t_i^e}$$

Total likelihood function,

$$L(\Theta_n; t^e, t^s, E^L, E^R, d_0) = \prod_{i=1}^{n_1} L_i^1 \prod_{j=1}^{n_2} L_j^2 \prod_{k=1}^{n_3} L_k^3 \prod_{i=1}^{n_1} L_i^{IP}$$

Maximum likelihood estimation (MSE)

Results

- **Parameter estimation**

Estimated incubation period

Mean: 5.8 (5.5, 6.0) days

Deviation: 1.8 (1.6, 2.1) days

Estimated mean generation time

12- 17 days

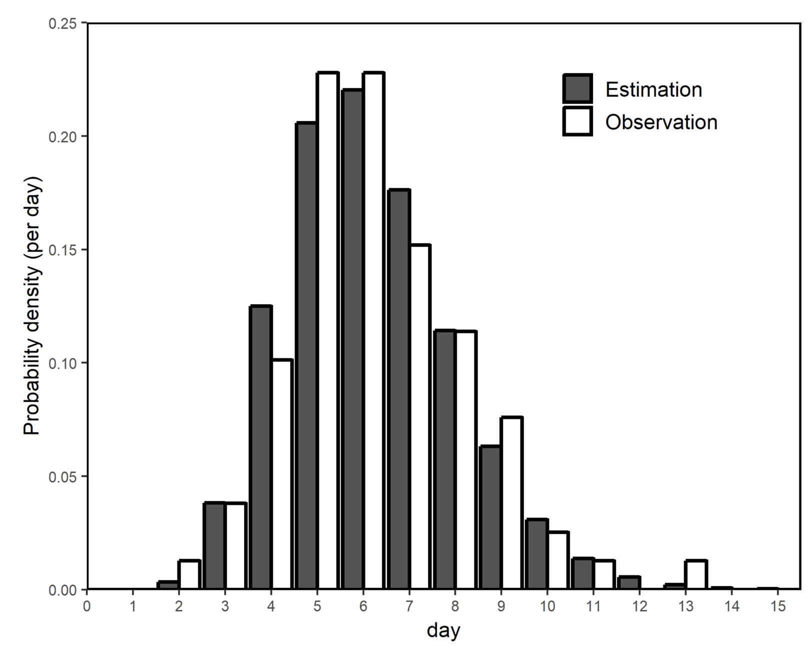


Fig 3. Probability distribution of incubation period

- **Model fitting with variable number of generations**

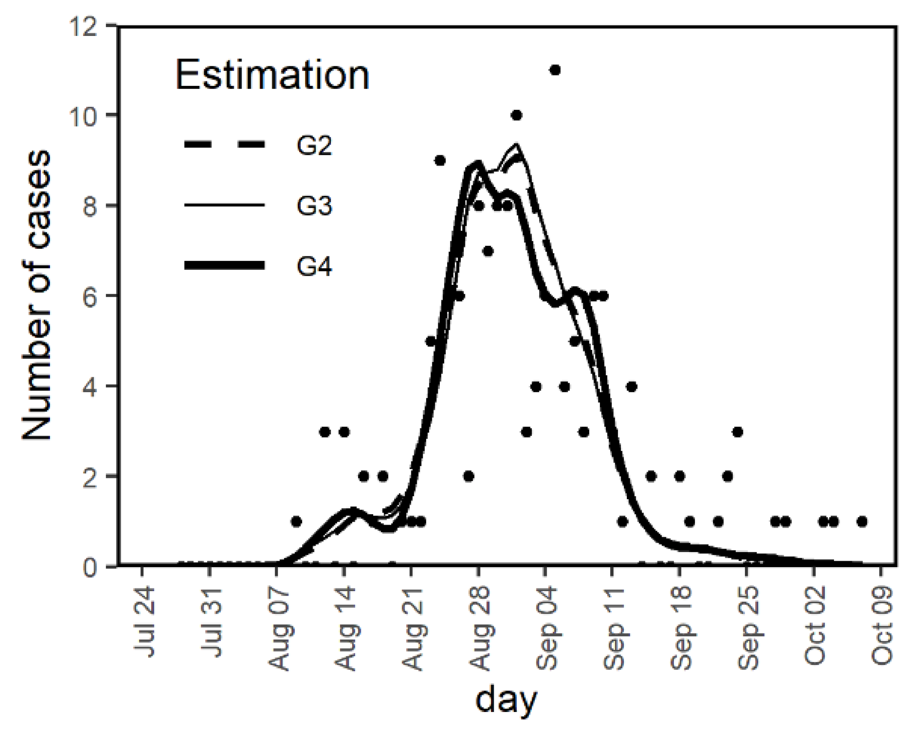


Fig 4. Comparison between observed and estimated epidemic curves with variable number of gnernation

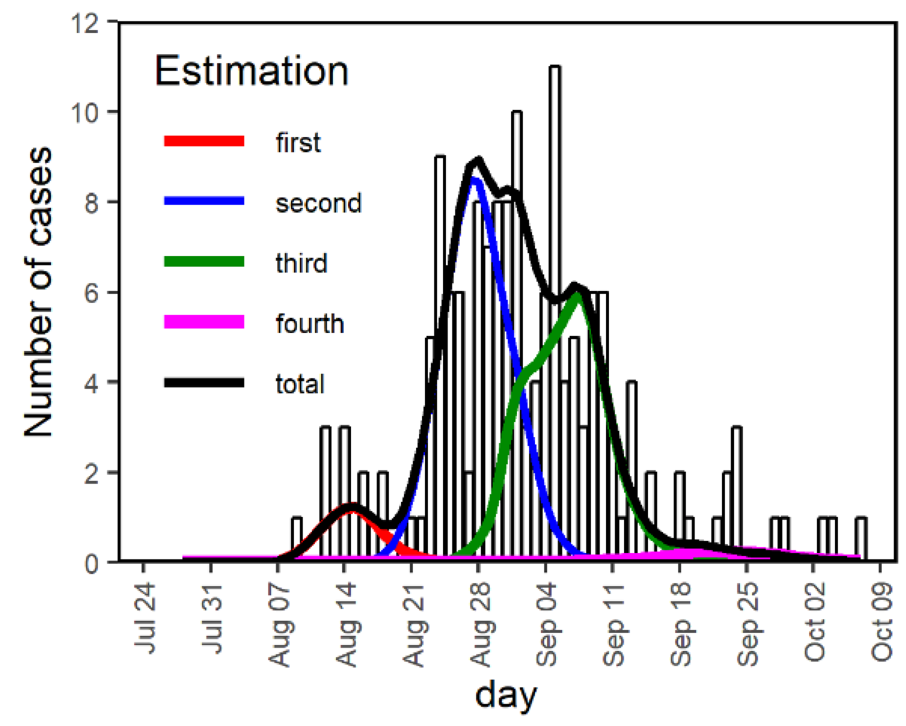


Fig 5. Comparison between observed and estimated epidemic curves with four generations

- **Effective reproduction number with variable number of generations**

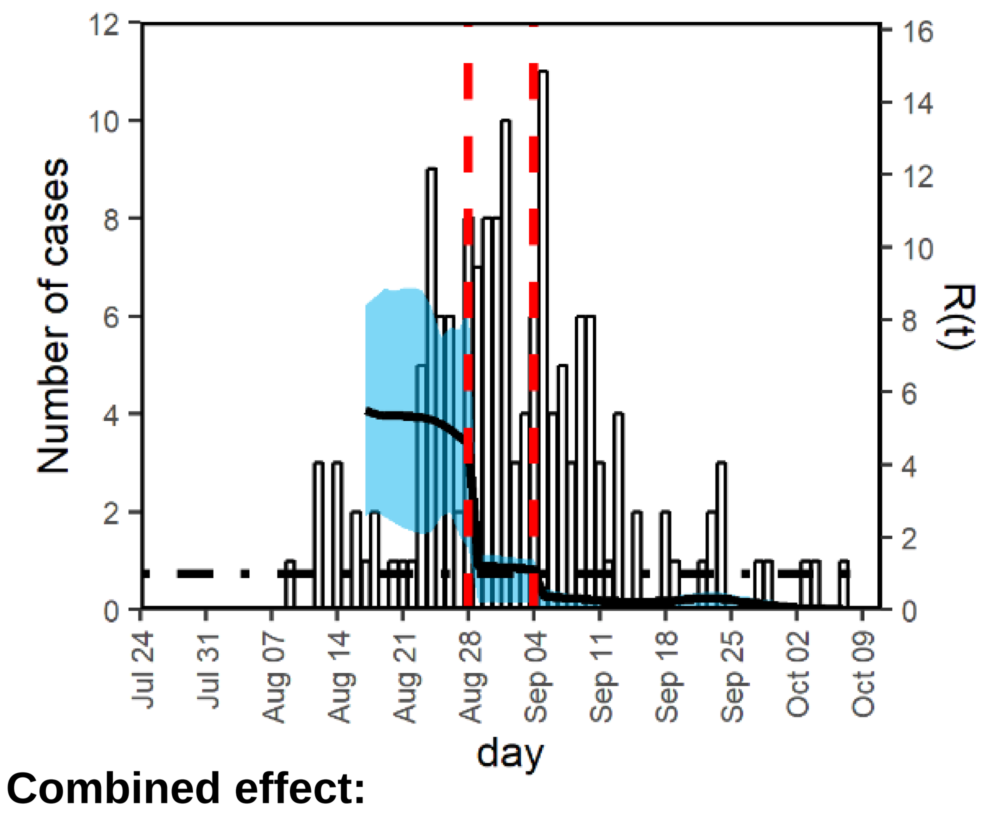


Fig 6. Estimated curve of the effective reproduction number with four genrations

Generation-dependent reproduction number (R_n):

R_0: 4.0 R_1: 5.4 (2.7, 10.5)

R_2: 4.3 (1.1, 16.8) R_3: 0.4 (0.2, 1.0)

Estimated $\varepsilon(t)$:

ε_1: 30%~70%; ε_2: 40%~80%

Combined effect:

The relative reduction in transmission rate due to combined interventaions $\varepsilon_1\varepsilon_2$: 44%~88%.

Discussion

- **A generation-dependent model was developed to parameterize the incidence of infection by convoluting the incidence of infection with the incubation period**
- **To fully halt virus transmission, the combined effect of mosquito control, public awareness campaigns, and park closure was needed for a substantial reduction in R_t**

[1] Bureau of Social Welfare and Public Health, Tokyo Metropolitan Government. 2014.

[2] Akhmetzhanov AR, et al. PLoS Curr. 2018; 10.