Characterization of H1N1 pandemic waves under various mitigation strategies

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Introduction

§ Multiple waves of morbidity and mortality over a few months or years are common characteristic of influenza pandemics.

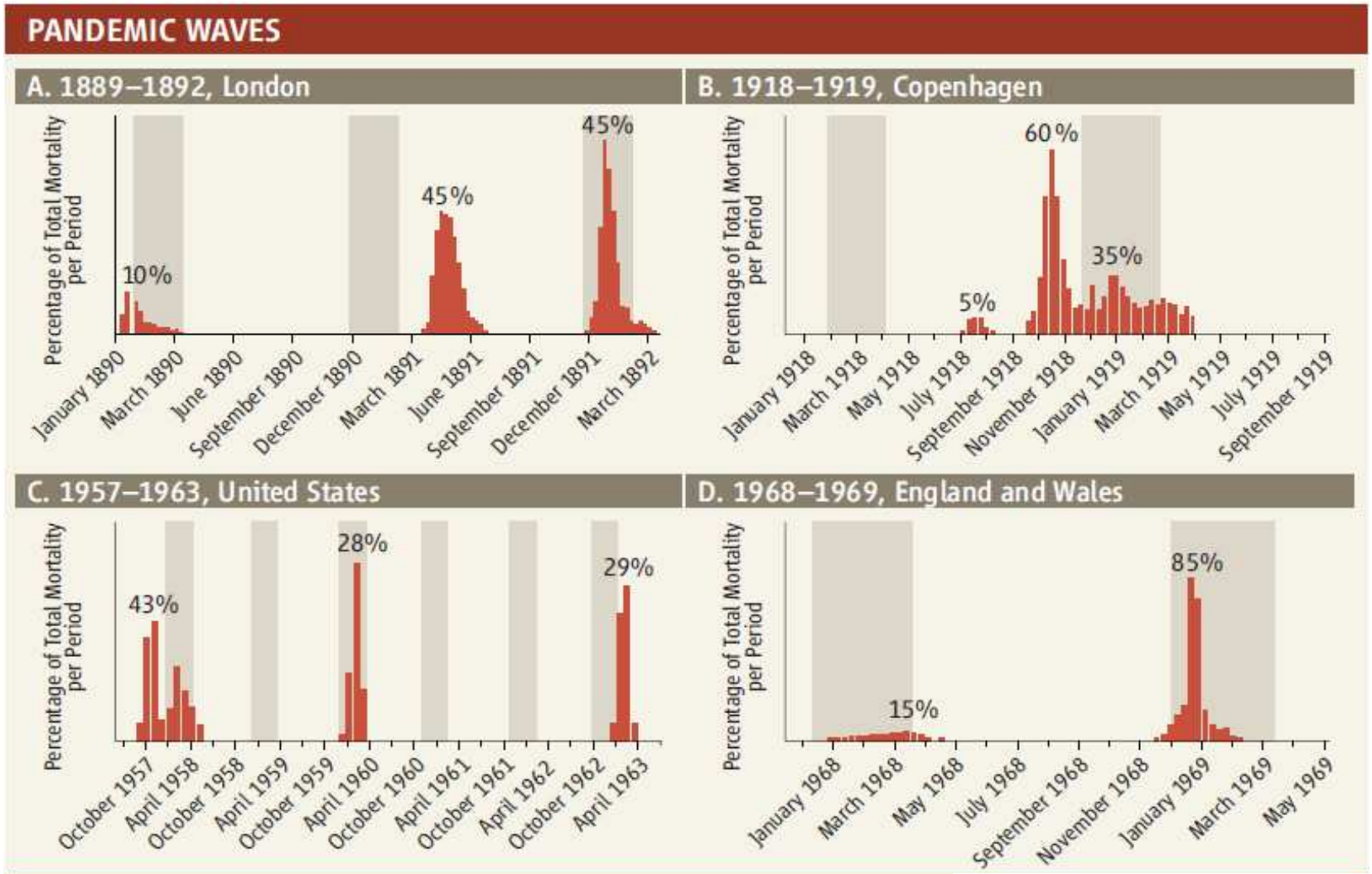
§ Size of these successive waves depend on the intervention strategies as well as the effects of immunity from prior infection.

§ Vaccination and antiviral drugs are the effective control measure for the containment of a pandemic.

§ Different countries adapt different control policies depending largely on their economic status and perhaps on the generosities of others.

§ **Objective** : To what extent are these control strategies effective in protecting populations from severe infection?

Past Pandemics waves



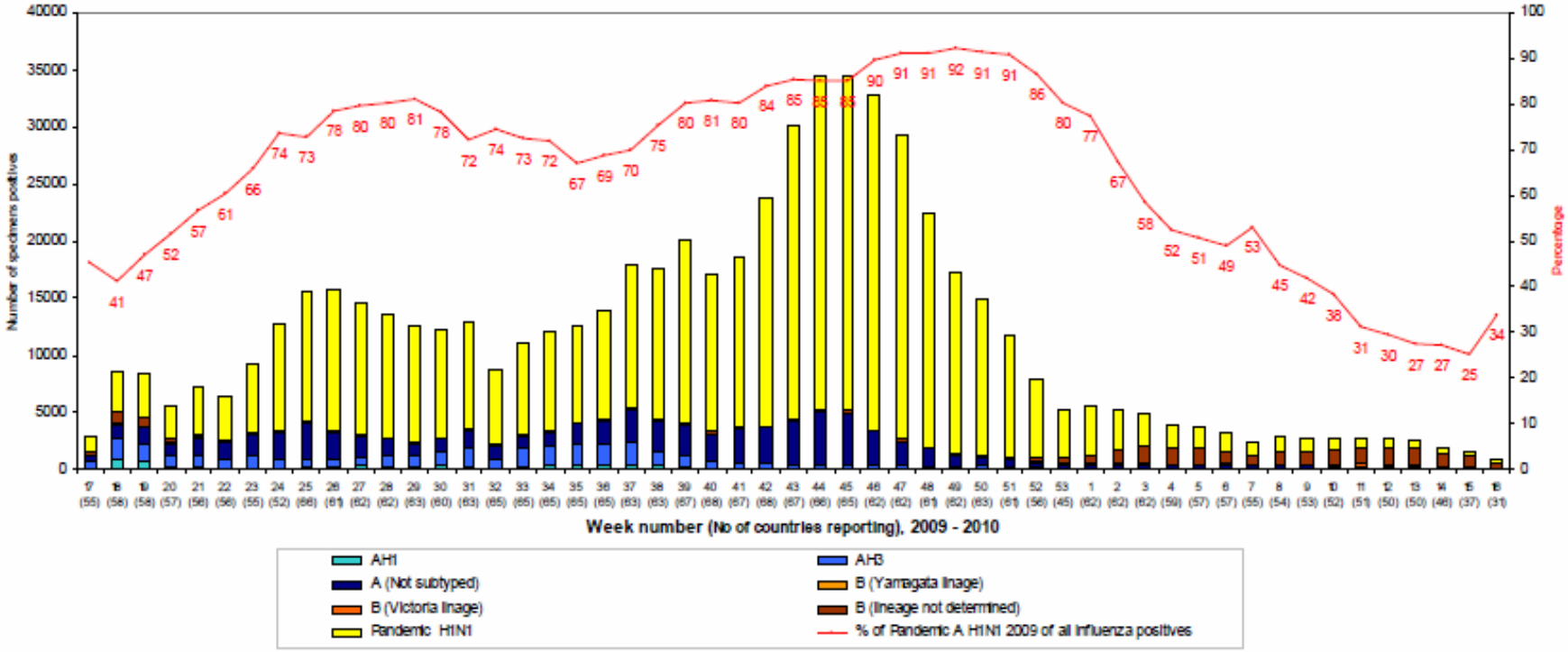
NEJM 360; 25 (2009)

H1N1 Pandemic 2009

Global circulation of influenza viruses

Number of specimens positives for influenza by subtypes

week 17 (2009) - 16 (2010) from 19 April 2009 to 24 April 2010



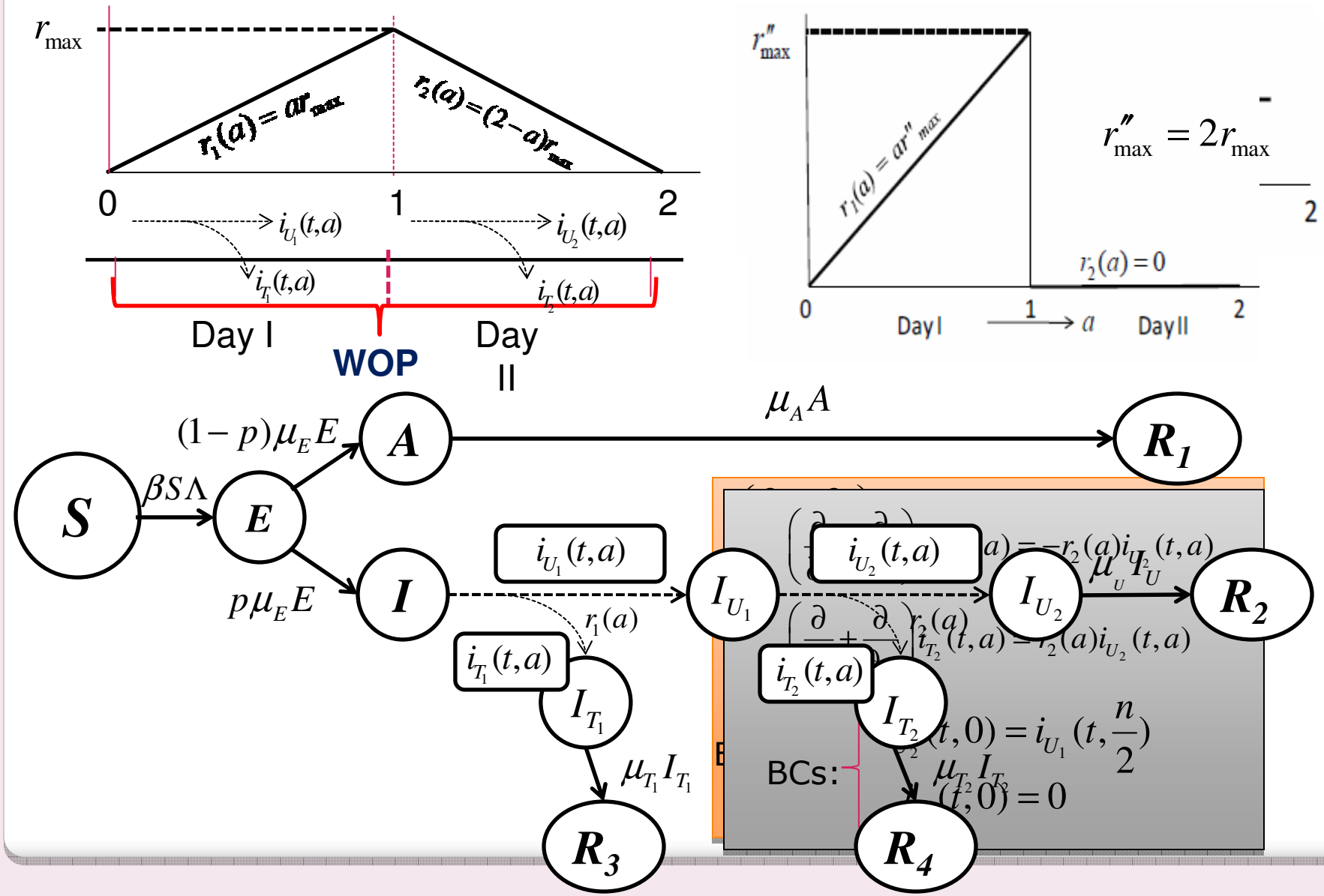
Data source: FluNet, Global Influenza Surveillance Network (GISN)

WHO

Antiviral stockpile size & no. of vaccine doses

Country	stockpile size (% population)	# doses vaccine (million)	vaccine uptake (% population)
Australia	41	21	30
Canada	25	50.4	40
China	1	100	3.2
France	50	94	7.8
UK	80	60	7
USA	30	195	20

Model Formulation (1st wave)



Model (1st wave)

$$
\begin{aligned}
\frac{dS}{dt} &= -\beta S\Lambda \\
\frac{dE}{dt} &= \beta S\Lambda - \mu_E E \\
\frac{dA}{dt} &= (1-p)\mu_E E - \mu_A A \\
\frac{dI_U}{dt} &= p\mu_E q_{\frac{n}{2}} E(t-n) q'_{\frac{n}{2}} - (\mu_U + d_U) I_U \\
\frac{dI_{T_1}}{dt} &= p\mu_E E(t-\frac{n}{2})(1-q_{\frac{n}{2}}) - (\mu_{T_1} + d_{T_1}) I_{T_1} \\
\frac{dI_{T_2}}{dt} &= p\mu_E q_{\frac{n}{2}} E(t-n)(1-q'_{\frac{n}{2}}) - (\mu_{T_2} + d_{T_2}) I_{T_2} \\
\frac{dR_1}{dt} &= \mu_A A \\
\frac{dR_2}{dt} &= \mu_U I_U \\
\frac{dR_3}{dt} &= \mu_{T_1} I_{T_1} \\
\frac{dR_4}{dt} &= \mu_{T_2} I_{T_2} .
\end{aligned}
$$

$$
\begin{aligned}
q_a &= e^{-\int_0^a r_1(x)dx}, \quad 0 \le a \le \frac{n}{2} \\
q'_a &= e^{-\int_{\frac{n}{2}}^{a+\frac{n}{2}} r_2(x)dx}, \quad 0 \le a \le \frac{n}{2}
\end{aligned}
$$

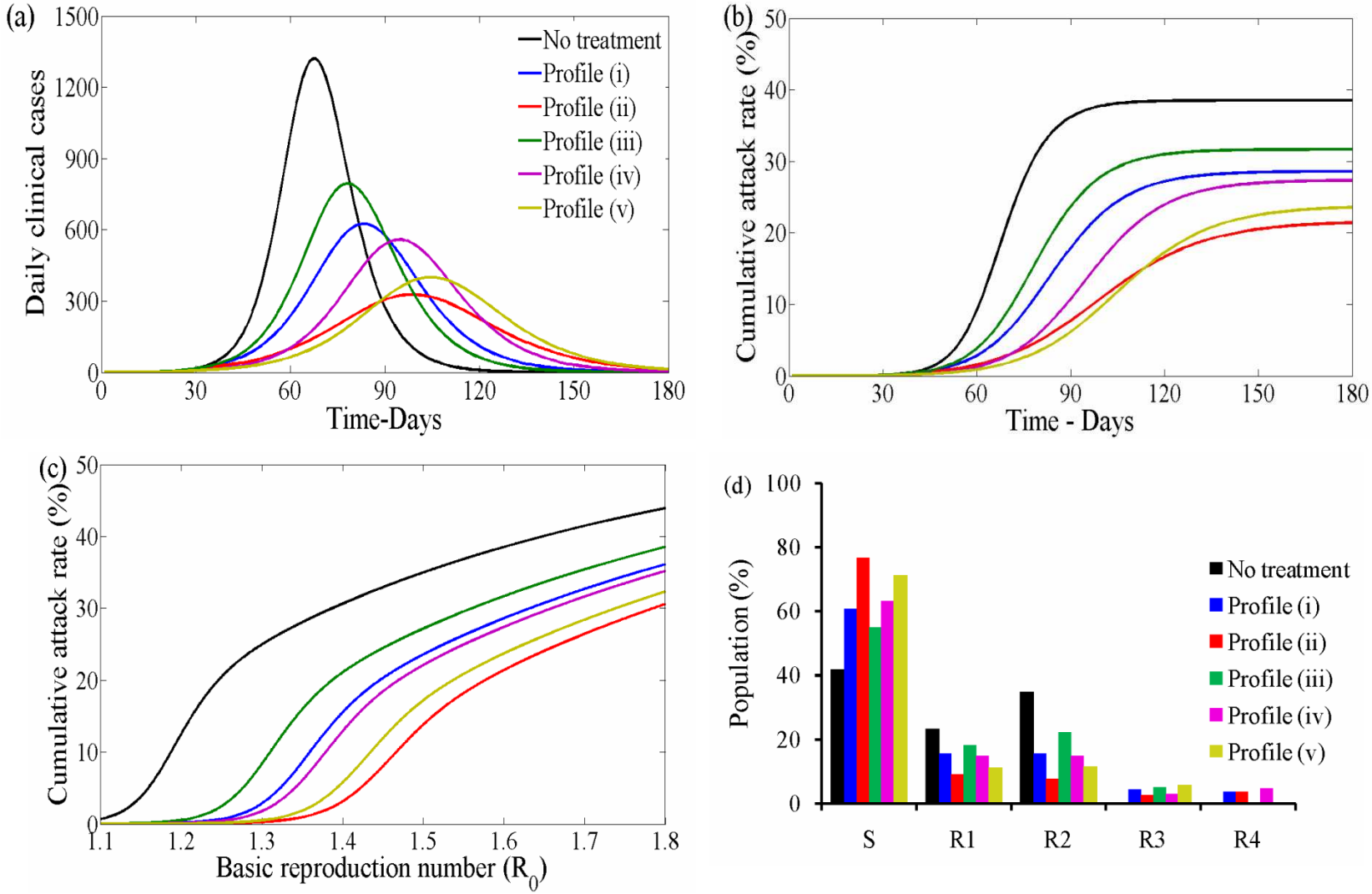
$$
\begin{aligned}
\Lambda &= \delta_A A(t) + \delta_U I_U(t) + \delta_U \delta_{T_1} I_{T_1} + \delta_U \delta_{T_2} I_{T_2} \\
&+ p\mu_E \int_0^{\frac{n}{2}} E(t-a)[q(a) + \delta_{T_1}(1-q(a))]da \\
&+ p\mu_E \int_{\frac{n}{2}}^{n} q_{\frac{n}{2}} E(t-\frac{n}{2}-a)[q'(a) + \delta_{T_2}(1-q'(a))]da
\end{aligned}
$$

Reproduction numbers (1st wave)

$$R_c = \beta S(0)\left[\begin{array}{l} \dfrac{(1-p)\delta_A}{\mu_A} + \dfrac{pq_{n/2}q'_{n/2}\delta_U}{\mu_U + d_U} + \dfrac{p(1-q_{n/2})\delta_{T_1}\delta_U}{\mu_{T_1} + d_{T_1}} \\ + \dfrac{pq_{n/2}(1-q'_{n/2})\delta_{T_2}\delta_U}{\mu_{T_2} + d_{T_2}} + p(\delta_{T_1} + \delta_{T_2})\dfrac{n}{2} \\ + p(1-\delta_{T_1})\displaystyle\int_0^{n/2} q(a)da + p(1-\delta_{T_2})\int_{n/2}^{n} q'(a)da \end{array}\right]$$

$$R_0 = \beta S(0)\left[\frac{(1-p)\delta_A}{\mu_A} + \frac{p\delta_U}{\mu_U + d_U} + np\right]$$

With & without treatment (1st wave)



Model (2nd wave)

$$\dot{q}_i = -\gamma_i \beta q_i \sum_{j=1}^{4} \sigma_j p_j, \quad i = *, 1, ..., 5$$

$$\dot{p}_1 = \sum_{i=*,1}^{5} [(1-\rho_i)\gamma_i \beta q_i \sum_{j=1}^{4} \sigma_j p_j] - \nu_1 p_1$$

$$\dot{p}_2 = \sum_{i=*,1}^{5} [\rho_i \gamma_i \beta q_i \sum_{j=1}^{4} \sigma_j p_j] - \phi_1 p_2 - \phi_2 p_2 - \nu_2 p_2$$

$$\dot{p}_3 = \phi_1 p_2 - \nu_3 p_3$$

$$\dot{p}_4 = \phi_2 p_2 - \nu_4 p_4$$

$$\dot{r} = \nu_1 p_1 + \nu_2 p_2 + \nu_3 p_3 + \nu_4 p_4$$

$$S = \sum_{i=*,1}^{5} q_i \quad I = \sum_{j=1}^{4} p_j \quad R = r$$

$$\gamma_i = \gamma, \quad \sigma_j = \sigma, \quad \nu_j = \nu,$$

$$\dot{S} = -\beta SI$$

$$\dot{I} = \beta SI - \nu I$$

$$\dot{R} = \nu I$$

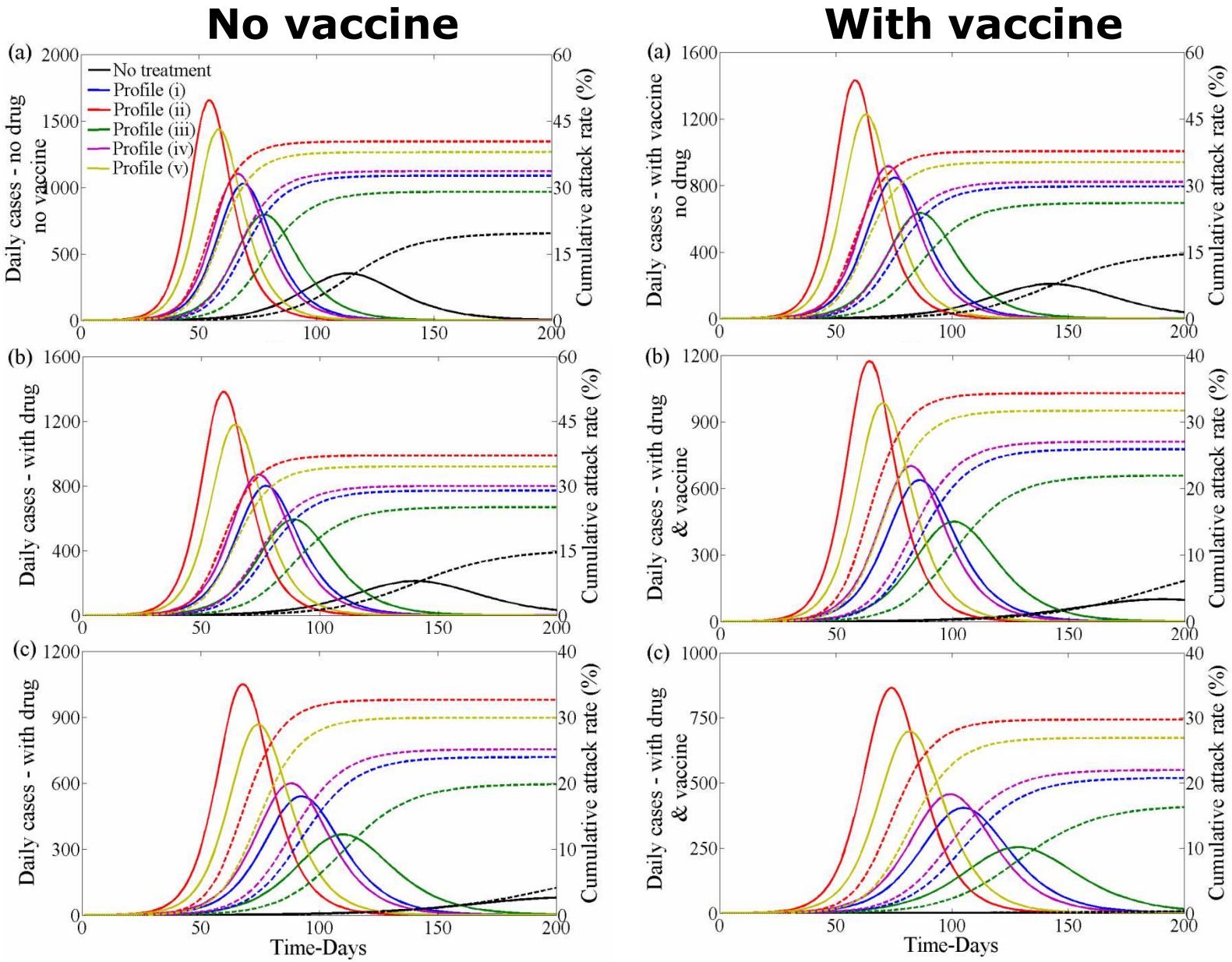
Reproduction numbers (2nd wave)

$$R_c = \beta \left[\frac{\sigma_1}{\nu_1} \sum_{i=*,1}^{5} \gamma_i q_i \frac{\sum_{i=*,1}^{5} (1-\rho_i)\gamma_i q_i}{\sum_{i=*,1}^{5} \gamma_i q_i} + \frac{\sigma_2}{\nu_2} \sum_{i=*,1}^{5} \gamma_i q_i \frac{\nu_2 \sum_{i=*,1}^{5} \rho_i \gamma_i q_i}{(\phi_1 + \phi_2 + \nu_2) \sum_{i=*,1}^{5} \gamma_i q_i} \right.$$
$$\left. + \frac{\sigma_3}{\nu_3} \sum_{i=*,1}^{5} \gamma_i q_i \frac{\phi_1 \sum_{i=*,1}^{5} \rho_i \gamma_i q_i}{(\phi_1 + \phi_2 + \nu_2) \sum_{i=*,1}^{5} \gamma_i q_i} + \frac{\sigma_4}{\nu_4} \sum_{i=*,1}^{5} \gamma_i q_i \frac{\phi_2 \sum_{i=*,1}^{5} \rho_i \gamma_i q_i}{(\phi_1 + \phi_2 + \nu_2) \sum_{i=*,1}^{5} \gamma_i q_i} \right]$$

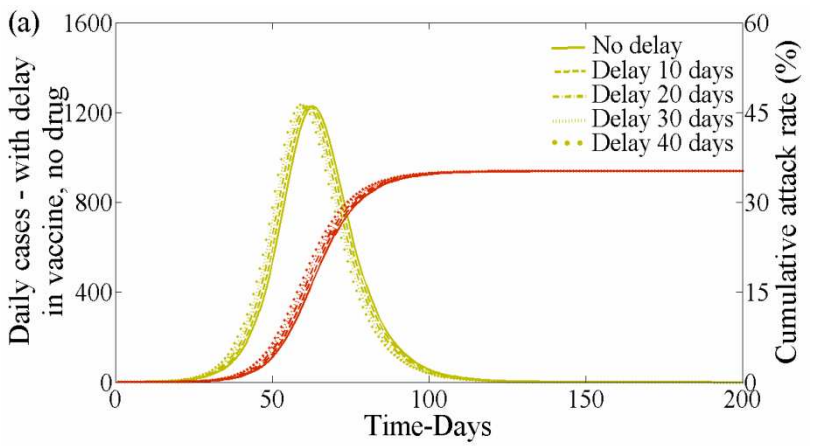
$$R_e = \frac{\beta \sigma_1}{\nu_1} \sum_{i=*,1}^{4} (1-\rho_i)\gamma_i q_i + \frac{\beta \sigma_2}{\nu_2} \sum_{i=*,1}^{4} \rho_i \gamma_i q_i$$

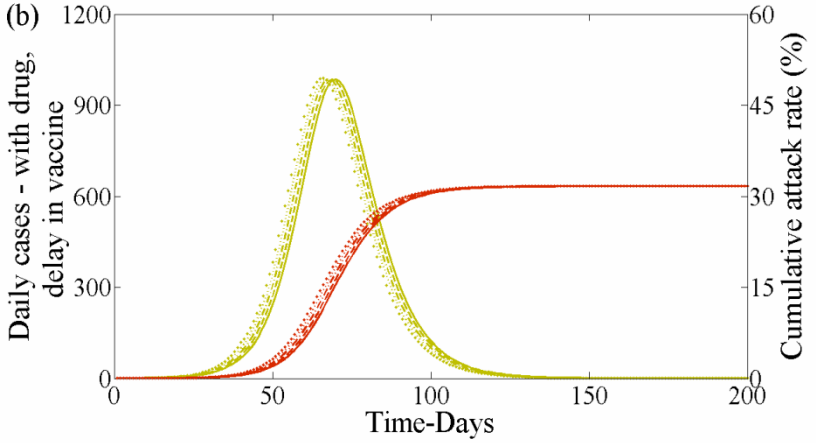
$$R_0 = \frac{(1-\rho)\beta \sigma_1}{\nu_1} + \frac{\rho \beta \sigma_2}{\nu_2}$$

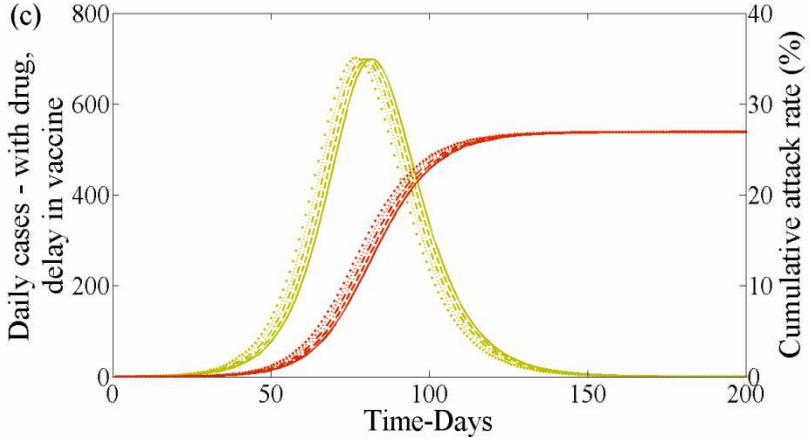
Clinical Infection (2nd wave)



Delay in vaccination

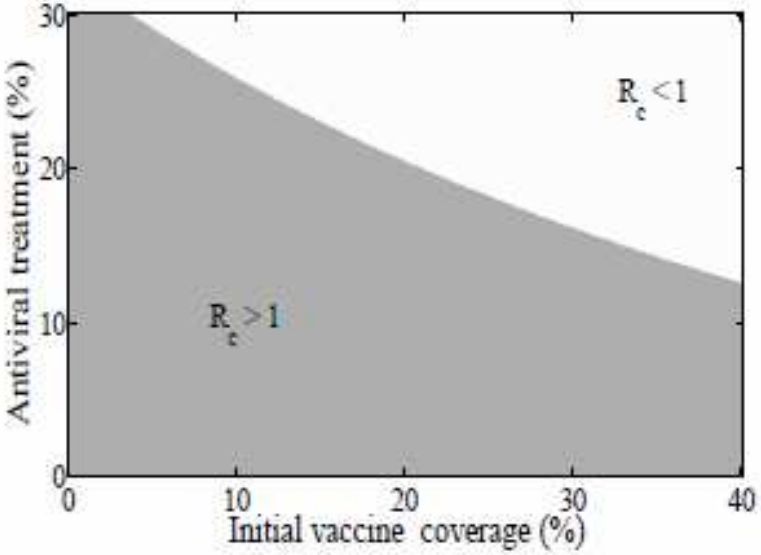




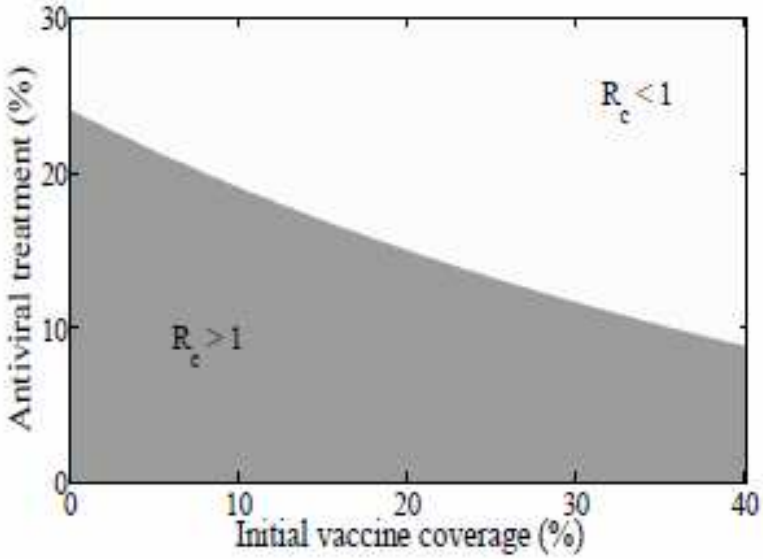


Effect of antiviral and vaccine

Treatment Profile (i)



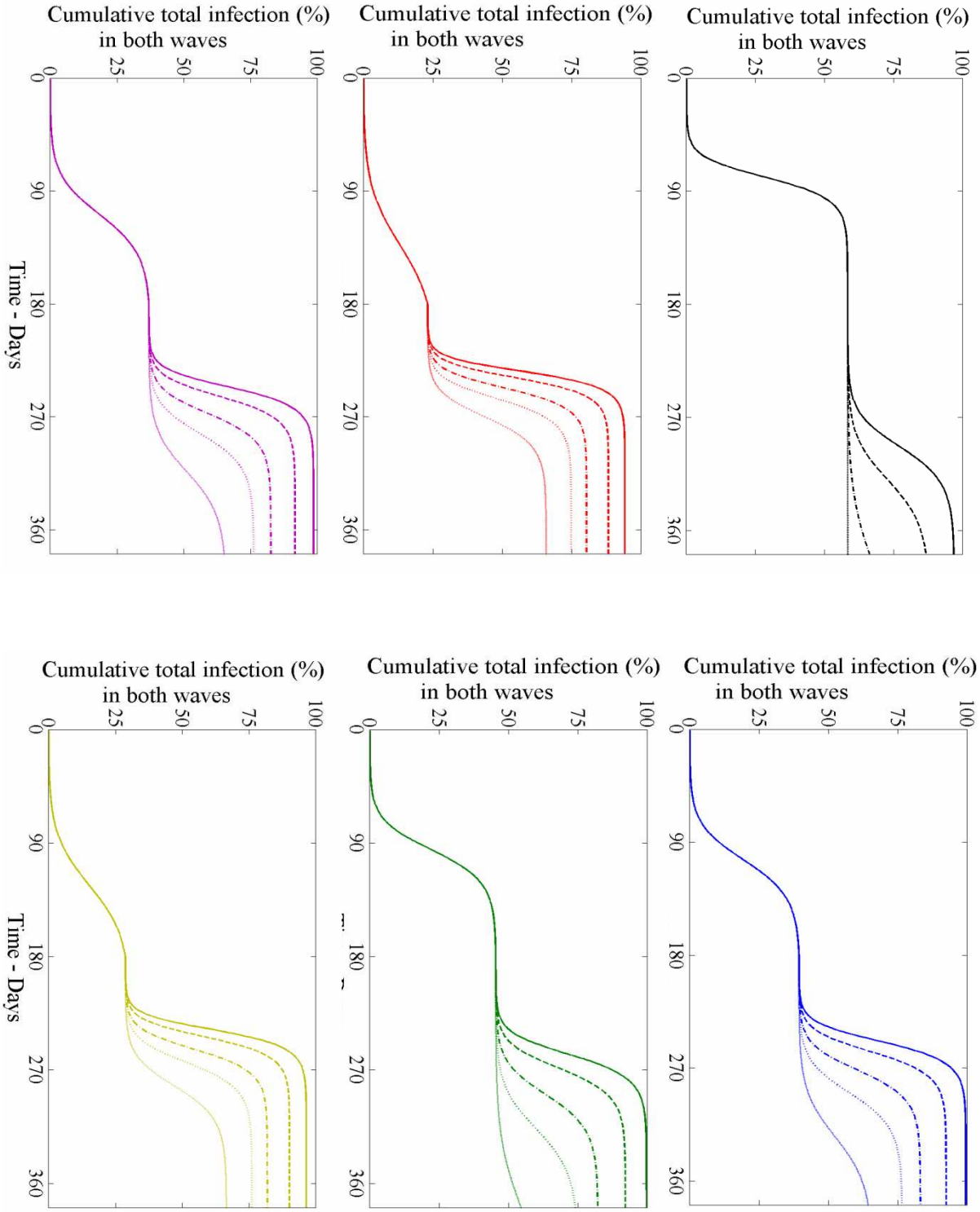
Treatment Profile (iii)



Cumulative infection & clinical cases

			Second wave no drug no vaccine	$< 5\%$ no vaccine	$> 5\%$ no vaccine	$< 5\%$ 30%	$> 5\%$ 30%
(a)	First wave	no treatment	96.7	86.7	66.2	58.4	58.3
		profile (i)	99.4	92.3	83.0	76.4	64.3
		profile (ii)	94.1	88.2	80.3	74.7	65.8
		profile (iii)	99.6	92.0	82.1	74.0	54.5
		profile (iv)	98.5	91.6	82.5	76.1	65.0
		profile (v)	96.3	90.0	81.7	75.9	66.5
(b)	First wave	no treatment	54.6	49.6	39.1	35.0	35.0
		profile (i)	56.2	52.5	47.5	43.2	36.9
		profile (ii)	54.1	50.9	46.5	42.3	37.5
		profile (iii)	56.2	52.3	47.0	42.1	32.0
		profile (iv)	55.8	52.1	47.2	42.9	37.2
		profile (v)	55.1	51.7	47.1	43.0	37.9

Cumulative - both waves



Conclusions

If drug therapy is readily available and vaccine is available in the second wave then the treatment profile (iii) in the first wave combined with this will result in the lowest number of possible infections in the population. No treatment in the first wave is optimal in most cases when drug stockpile is limited, drug therapy use is low and if vaccination is not available.

Important implications to public health initiatives to identify best population based strategies on the availability of vaccine and antivirals.

These results pertain to the population setting. The best result for an individual in the population is to stave off severe infection. The benefits of the individual against population will be weighed.

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