Modelling infectious diseases with herd immunity in a randomly mixed population

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Research Article

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Abstract

Background

The conventional susceptible-infectious-recovered (SIR) model tends to overestimate the transmission dynamics of infectious diseases and ends up with total infections and total immunized population exceeding the threshold required for control and eradication of infectious diseases. The study aims to overcome the limitation by allowing the transmission rate of infectious disease to decline along with the reducing risk of contact infection.

Methods

Two new SIR models were developed to mimic the declining transmission rate of infectious diseases at different stages of transmission. Model A mimicked the declining transmission rate along with the reducing risk of transmission following infection, while Model B mimicked the declining transmission rate following recovery. Then, the conventional SIR model, Model A and Model B were used to simulate an infectious disease with a basic reproduction number (r_0) of 3.0 and a herd immunity threshold (HIT) of 0.667 with and without vaccination. The infectious disease was expected to be controlled or eradicated when the total immunized population either through infection or vaccination reached the level predicted by the HIT. Outcomes of simulations were assessed at the time when the total immunized population reached the level predicted by the HIT, and at the end of simulations.

Findings

All three models performed likewise at the beginning of the transmission when sizes of infectious and recovered were relatively small as compared with the population size. The infectious disease modelled using the conventional SIR model appeared completely out of control even when the HIT was achieved in all scenarios with and without vaccination. The infectious disease modelled using Model A appeared to be controlled at the level predicted by the HIT in all scenarios with and without vaccination. Model B projected the infectious disease to be controlled at the level predicted by the HIT only at high vaccination rates. At lower vaccination rates or without vaccination, the level at which the infectious disease was controlled cannot be accurately predicted by the HIT.

Conclusion

Transmission dynamics of infectious diseases with herd immunity can accurately be modelled by allowing the transmission rate of infectious disease to decline along with the combined risk of contact infection. Model B provides a more credible framework for modelling infectious diseases with herd immunity in a randomly mixed population.

Funding

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Keywords

Herd immunity; Deterministic model; Vaccine; Vaccination; Population immunity; Herd immunity threshold

Introduction

Herd or population immunity refers to the indirect protection from infectious diseases among remaining susceptible individuals when most people in a population are immune to infectious diseases either through vaccination or infection. The concept of herd immunity became a fixture of epidemiology in 1930s, and took on fresh prominence in 1950s and 1960s as new vaccines raised crucial questions for public health policy on the proportion of the vaccinated population for the eradication of infectious diseases[1]. Herd immunity takes effect when the transmission rate of infectious diseases starts to decline along with the reducing risk of infection due to the presence or proximity of immune individuals in a randomly mixed population[2]. Although the effect of herd immunity has been observed in many vaccinated populations of periodical childhood epidemics, such as measles, mumps, rubella, pertussis, chickenpox and polio, it has not been successfully attained through mathematical modelling.

Mathematical models such as the susceptible-infectious-recovered (SIR) and its variants are widely used to simulate the transmission pattern of infectious diseases. Those models use a flexible compartmental framework with robust assumptions for a wide range of applications[3–6]. The compartmental framework of SIR model simplifies the transmission dynamics of infectious diseases by classifying individuals based on their epidemiological status and ability to host and transmit a pathogens[7]. Other than the framework, the SIR model also assumes complete immunity can be acquired through infection, hence encompassing the epidemiological notion of herd immunity through infection[8,9].

It is generally believed that infectious diseases can be controlled or eradicated when the total immunized population reaches a level predicted by the herd immunity threshold (HIT). The HIT indicates a level of one infected individual generating less than one secondary case on average[10]. The transmission of infectious diseases becomes unsustainable in a population beyond the HIT. The HIT can be calculated from the basic reproduction number (r_0) of infectious diseases to guide the vaccination strategy for controlling an epidemic or pandemic, either through vaccine or infection[2,11]. For instance, to control or eradicate the COVID-19 pandemic, vaccination should cover 50.0% to 66.7% of the world population based on the r_0 of 2.0 to 3.0 for the novel coronavirus[12–15].

The conventional SIR model often overestimates the transmission dynamics of infectious diseases. For instance, an infectious disease with r_0 of 3.0 would eventually infect up to 94.0% of a population, a level way beyond the expected HIT, even with the presence of herd immunity if modelled using the conventional SIR model. This problem is of great concern especially for time being as many models have been developed based on the conventional SIR framework to guide public health planning and preparedness against the COVID-19 pandemic[16–19]. This study aims to investigate and overcome the aforesaid limitation of using the SIR model in modelling infectious diseases with herd immunity in a randomly mixed population. We proposed a key modification to the conventional SIR model that allows the transmission rate of infectious disease to decline along with the reducing risk of contact infection, which is more in line with the principle of herd immunity.

Methods

Conventional SIR model

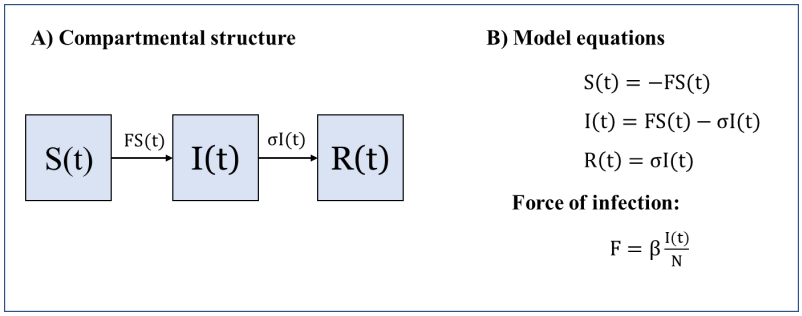

Figure 1: The compartmental structure and model equations of Kermack & Mckendrick's SIR model.

Kermack & McKendrick postulated the first SIR model for infectious diseases in 1927 before vaccines became popular in 1950s for control and eradication of infectious diseases[9]. Then, the SIR model became the fundamental of most infectious disease models developed. The conventional SIR model divides a homogenous population, N into three basic compartments: susceptible denoted by S(t), infectious denoted by I(t), and recovered or removed denoted by R(t), and assumes infectious diseases spread from affected to unaffected through contact infection (Fig.1). Susceptible are individuals who have an equal risk of being infected. Infectious are individuals who have developed infectivity and can transmit pathogen to those who remain susceptible. Recovered or removed are individuals who have recovered from infection and immune to reinfection. In brief, the conventional SIR model describes the transmission of infectious disease with herd immunity through infection. The SIR model can be described mathematically by a set of ordinary differential equations (ODEs) as shown in Fig. 1.

According to model equations (Fig. 1), the rate of individuals moving from compartment S(t) to I(t) due to contact infection is determined by S(t) and the force of infection, F, which consists of the product of a constant contact rate (β) and the proportion of infectious individuals, $\frac{I(t)}{N}$. And, the rate of individuals moving from compartment I(t) and R(t) following recovery is determined by I(t) and the reciprocal of infection duration, denoted by σ. Therefore, the conventional SIR model often simulates the I(t) to increase at the beginning of transmission and subsequently diminishes due to the exhausting stock of S(t).

Without vital dynamics, the population size is constant and can be given by:

$$N = S(t) + I(t) + R(t) \quad (1)$$

Equation (1) can be converted into prevalence or proportion by dividing each notation with the population size, N:

$$1 = \frac{S(t)}{N} + \frac{I(t)}{N} + \frac{R(t)}{N}. \quad (2)$$

According to Equation (2), I(t) and R(t) are often very small as compared with N at the beginning of the transmission, therefore, $\frac{I(t)}{N} \approx 0$, $\frac{R(t)}{N} \approx 0$, and $\frac{S(t)}{N} \approx 1$. At the end of transmission, the I(t) would become very small again, therefore, $1 - \frac{R(t)}{N} \approx \frac{S(t)}{N}$. To model infectious diseases with herd immunity, $\frac{S(t)}{N}$ or $1 - \frac{R(t)}{N}$ can be incorporated into the force of infection to mimic the reducing risk of contact infection at different stages of infection.

By incorporating $\frac{S(t)}{N}$ into the F, we assume herd immunity takes effect to reduce the transmission rate of infectious diseases along with the reducing risk of contact infection following infection. By incorporating $1 - \frac{R(t)}{N}$ into the F, we assume herd immunity takes effect to reduce the transmission rate of infectious diseases along with the reducing risk of contact infection following recovery.

New SIR models

In chemistry, the Law of Mass Action is used to describe the rate of chemical reactions being proportional to the concentration of reactants.[20] Based on the above principle, a contact can be regarded as an interactive event between susceptible individuals and infectious individuals in a randomly mixed environment, with its rate being proportional to $\frac{S(t)}{N}$ and $\frac{I(t)}{N}$. The product of $\frac{S(t)}{N}$ and $\frac{I(t)}{N}$ denotes the combined risk of contact infection. Two new models were developed based on the above principle as below:

Model A: The total transmission rate of infectious diseases in a randomly mixed population depends on the S(t) and a new force of infection, F_A, which consists of the product of β, $\frac{I(t)}{N}$ and $\frac{S(t)}{N}$ as follow:

$$F_A = \beta \frac{I(t)S(t)}{N^2}. \quad (3)$$

In Model A, the risk of contact infection is determined by both $\frac{S(t)}{N}$ and $\frac{I(t)}{N}$. Therefore, the transmission rate would decline along with the reducing risk of contact infection when individuals move from compartment S(t) to I(t) due to infection. The compartmental structure and model equations of Model A can be found in Fig. 2.

Model B: The total transmission rate of infectious diseases in a randomly mixed population depends on the S(t) and a new force of infection, F_B, which consists of the product of β, $\frac{I(t)}{N}$ and $1 - \frac{R(t)}{N}$ as follow:

$$F_B = \beta \frac{I(t)[N - R(t)]}{N^2}. \quad (4)$$

In Model B, the risk of contact infection is determined by both $1-\frac{R(t)}{N}$ or $\frac{N-R(t)}{N}$ and $\frac{I(t)}{N}$. Therefore, the transmission rate would decline along with the reducing risk of contact infection when individuals move from compartment I(t) to R(t) after recovery. The $1-\frac{R(t)}{N}$ denotes the inverse of proportion of recovered individuals and is used to mimic the reducing risk of contact infection following recovery. The compartmental structure and model equations of Model B can be found in Fig. 2.

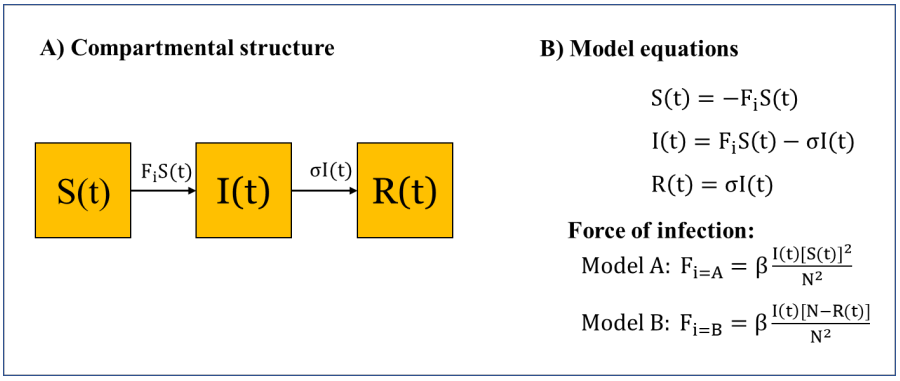

Figure 2: The compartmental structure and model equations of the newly developed Model A and Model B.

Both Model A and Model B retain the basic SIR compartmental structure, except for the force of infection (Fig. 2). With the modification, both models can be used to simulate the transmission dynamics of infectious diseases with herd immunity through infection in a randomly mixed population.

The basic reproduction number, r_0

The equation of I(t) from the conventional SIR model, Model A and Model B can be rearranged as follows:

$$\frac{dI(t)}{dt} = \left[\beta\frac{S(t)}{N} - \sigma\right] I(t)\ . \qquad (5)$$

$$\frac{dI(t)}{dt} = \left[\beta\left(\frac{S(t)}{N}\right)^2 - \sigma\right] I(t)\ . \qquad (6)$$

$$\frac{dI(t)}{dt} = \left[\beta\left(\frac{S(t)[N-R(t)]}{N^2}\right) - \sigma\right] I(t)\ . \qquad (7)$$

At the beginning of the transmission, when $\frac{S(t)}{N} \approx 1$ and $\frac{R(t)}{N} \approx 0$, we would obtain the exact equation for all three models as follow:

$$\frac{dI(t)}{dt} = (\beta - \sigma)I(t). \qquad (8)$$

The integral of Equation (8) is an exponential function as follow:

$$I(t) = I_0 e^{(\beta-\sigma)t}. \quad (9)$$

Equation (9) shows a crucial condition that determines the widespread of infectious diseases in a population. The transmission of infectious diseases can be sustained if $\beta > \sigma$ or $\frac{\beta}{\sigma} > 1$. The ratio between β and σ denotes the basic reproduction number (r_0) of infectious diseases. The r_0 can also be defined as the number of secondary cases caused by a single primary case in a wholly susceptible population[21,22]. The r_0 can be used to derive the herd immunity threshold (HIT) according to a simple theorem proposed by Dietz (1975)[23].

$$HIT = 1 - \frac{1}{r_0}. \quad (10)$$

The HIT can also be defined as the level that the transmission of infectious diseases becomes unsustainable when one infected person generates less than one secondary case on average in a population[10]. Often, the HIT can be used to predict total infections achieved at the end of transmission without vaccination. If vaccination is used to control infectious diseases, the HIT indicates the share of a population that needs to be vaccinated for control of infectious diseases.

Vaccine models

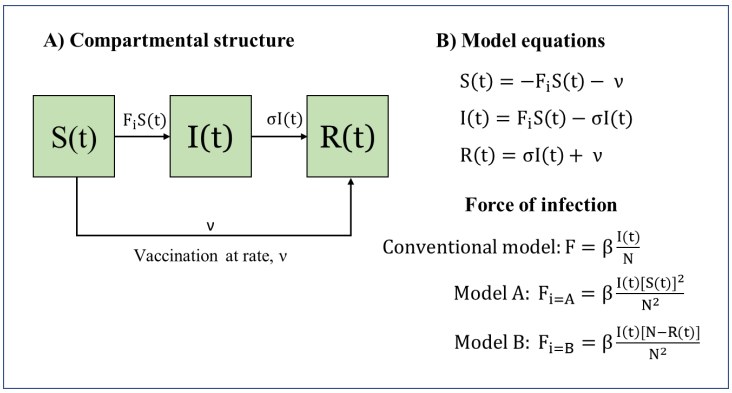

Figure 3: The compartmental structure and model equations of vaccine models modified using the conventional SIR model, Model A and Model B.

Unlike immunity through infection, vaccination introduces immunity into individuals without developing infectivity, therefore protecting a population from infectious diseases without generating more infections. A simple vaccine model can be created using the conventional SIR model, Model A and Model B by allowing individuals vaccinated to move from compartment S(t) straight to R(t) at a constant vaccination rate denoted by ν (Fig. 3). The magnitude of ν depends on factors such as the availability of vaccines and resources allocated for vaccinating people, not the size of S(t). Here, we assume individuals who have been vaccinated would develop complete immunity as those developing immunity through infection. Therefore, the compartment R(t) would consist of the total immunized population either through infection or vaccination. Herd immunity was considered achieved when the total immunized population reached the level predicted by the HIT.

Table 1 shows the breakdown of transmission rate and recovery rate of the conventional SIR model, Model A and Model B. Model A and Model B only differ from the conventional SIR

model in the risk of contact infection. By assigning the same value to β, σ and ν, all three models can be used to simulate the transmission dynamics of the same infectious disease with herd immunity either through infection or vaccination in a randomly mixed population.

Table 1: Breakdown of transmission rate and recovery rate of the conventional SIR model, Model A and Model B.

Models	Components of transmission rate			Total transmission rate from S(t) to I(t)	Components of recovery rate		Total recovery rate from I(t) to R(t)	Vaccination rate
	Force of infection, F		Number of Susceptible					
	Contact rate	Risk of contact infection			Recovery coefficient	Number of Infectious		
Conventional SIR model	β	$\frac{I(t)}{N}$	S(t)	$\beta\frac{I(t)S(t)}{N}$	σ	I(t)	σI(t)	ν
Model A	β	$\frac{I(t)S(t)}{N^2}$	S(t)	$\beta\frac{I(t)[S(t)]^2}{N^2}$	σ	I(t)	σI(t)	ν
Model B	β	$\frac{I(t)[N-R(t)]}{N^2}$	S(t)	$\beta\frac{I(t)S(t)[N-R(t)]}{N^2}$	σ	I(t)	σI(t)	ν

Simulations and sensitivity analyses

Model ODEs of all three models can be solved by using numerical integration. First, we simulated all three models under the exact and arbitrary conditions with parameter values as presented in Table 2. These parameter values allowed all three models to project the transmission dynamics of the same infectious disease in a homogenous population. We assumed complete immunity can be acquired either through infection or vaccination, therefore, herd immunity can be developed either through infection or vaccination. Herd immunity was considered achieved when the total immunized population reached the level predicted by the HIT.

Transmission dynamics of the infectious disease with herd immunity through infection only were simulated using models as presented in Fig. 1 and Fig. 2. We expected the infectious disease to subside when the total immunized population or R(t) reached the level predicted by the HIT. We evaluated the size of each compartment at the time when the HIT was reached, and at the end of simulation (t=200).

Transmission dynamics of the infectious disease with herd immunity through vaccination and infection were simulated using models as presented in Fig. 3. The total immunized population would consist of those who had developed immunity through infection or vaccination. At high vaccination rates, the total immunized population was largely contributed by those acquiring immunity through vaccination. At low vaccination rates, the total immunized population was largely contributed by those acquiring immunity through infection. We simulated all vaccine models at three vaccination rates, as stated in Table 2. At all vaccination rates, we evaluated the size of each compartment at the time when the HIT was reached, and at the end of simulations (t=500 for ν=1.0%, t=300 for ν=0.5%, and t=200 for ν=0.1%). The vaccination rate was set to zero after the HIT was reached until the end of simulations.

In sensitivity analyses, we evaluated total infections generated by all three models at the end of simulation across r_0 from 1.1 to 4.0 without vaccination. Numerical integrations and simulations were performed in R version 3.6.3 by using "deSolve" package. Graphics were generated by using Microsoft Excel 2019.

Table 2: Parameter values used in simulations and sensitivity analyses

Parameters	Values
Contact rate, β	0.3 0.11 to 0.4 (Sensitivity analysis)
Recovery coefficient, σ	0.1
Infection duration	10
Basic reproduction number, r_0	3.0 1.1 to 4.0 (Sensitivity analysis)
Herd immunity threshold, HIT	0.667 (66.7%)
Vaccination rate, ν	1.0% population per unit t 0.5% population per unit t 0.1% population per unit t
Population size, N	1000000
Initial value for I(t)	1
Initial value for S(t)	N-I(t)
Initial value for R(t)	0
Initial value for Total infections	1

Results:

Transmission dynamics of infectious diseases with herd immunity through infection

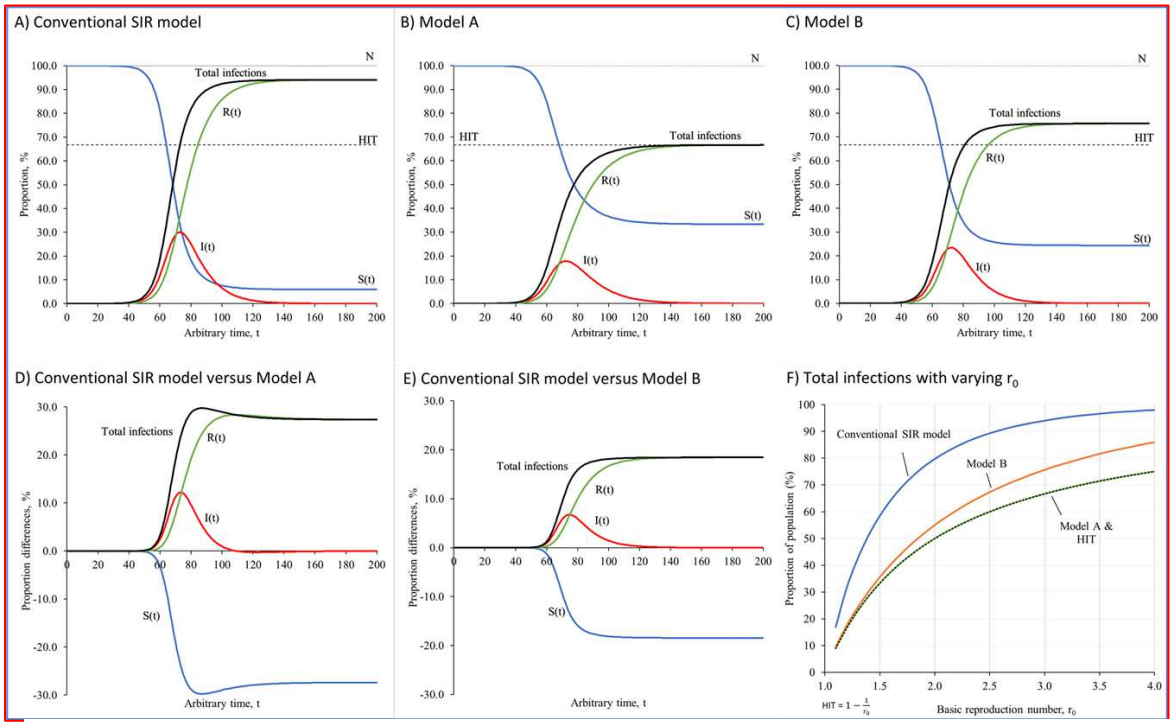

Figure 4: Transmission dynamics of infectious diseases with herd immunity through infection
Part A, B and C presents transmission dynamics of infectious diseases with herd immunity through infection simulated by the conventional SIR model, Model A and Model B. Part D and E presents proportion differences between the conventional SIR model and Model A and between the conventional SIR mode and Model B. Part F presents total infections generated by the conventional SIR model, Model A and Model B with varying r_0.

Without vaccination, all three models described the transmission dynamics of infectious diseases with herd immunity through infection as individuals who had been infected were assumed to recover with complete immunity. Figure 4 presents the transmission dynamics of infectious disease with r_0 of 3.0 simulated using the conventional SIR model, Model A and Model B. Our simulations showed that all three models performed likewise at the beginning of the transmission when both I(t) and R(t) were relatively small as compared with the population size, N.

According to the conventional SIR model, the total R(t) or immunized population through infection would reach the level predicted by the HIT at t=134, with total infections reaching 86.9%, I(t) reaching 19.2% and S(t) reaching 13.1%. After that, the infectious disease would continue to infect more people, and ended up with up to 94.0% of population being infected, leaving only 6.0% of population remaining susceptible (Fig. 4A and Table 3). Model A projected the infectious disease to be controlled and eradicated at the level accurately predicted by the HIT at t=195 until the end of simulation (Fig. 4B and Table 3). Model B projected the infectious disease to subside at a level higher than the HIT, with total infections reaching 75.6%, leaving 24.4% of population to remain susceptible in the population (Fig. 4C and Table 3).

According to our simulations, the transmission of infectious disease started to be controlled and suppressed after t=50 in both Model A and Model B as compared with the conventional SIR model (Fig. 4D and 4E). Our sensitivity analysis shows that total infections generated by the conventional SIR model at the end of simulation were completely way above the level predicted by the HIT across all r_0 values. Total infections generated by Model A at the end of simulation were accurately predicted by the HIT across all r_0 values, while total infections generated by Model B at the end of simulation were predicted the HIT when r_0 was small and deviated away from the HIT at higher r_0 values in Model B (Fig. 4F).

By allowing the transmission rate to decline along with the reducing risk of contact infection, Model A simulated the infectious disease to subside at a level predicted by the r_0 and HIT accurately. However, it might be too ideal to assume that the risk of contact infection and transmission rate can be reduced by herd immunity immediately following infection, unless in the context of high vaccination rates. Model B was more in line with the fundamental of herd immunity. It was more realistic to allow the transmission rate to decline along with the reducing risk of contact infection following recovery.

Transmission dynamics of infectious diseases with herd immunity through vaccination

With modification as shown in Fig.3, all three models can be used to describe the transmission dynamics of infectious diseases with herd immunity through vaccination. At a very high vaccination rate (ν=1.0% population per unit t), our simulations showed that total infections would continue to increase at a lower rate even after the HIT was achieved in the conventional SIR model (Fig. 5A). The conventional SIR model failed to demonstrate either control or eradication of infectious diseases even at a high vaccination rate after the HIT was achieved, let alone lower vaccination rates. On the other hand, both Model A and Model B projected the infectious disease to be controlled and eradicated when the total immunized population reached

the level predicted by the HIT. At a very high vaccination rate, both Model A and Model B performed likewise and generated the same outcome with total infections controlled at 0.02% after the HIT was achieved at t=67 until the end of the simulation (Fig. 5B and 5C, Table 3).

At a lower vaccination rate (ν=0.5% population per unit t), total infections continued to increase at a higher rate even after the HIT was achieved at t=100 in the conventional SIR model (Fig. 5D, Table 3). At t=100, the total immunized population reached 67.58% of population, consisting of 18.08% of population immunized through infection and 49.50% of population immunized through vaccination. The infectious disease appeared completely out of control and continued to infect more people in the population, causing total infections to increase by another 8.06% and reached 34.37% at the end of simulation (t=500). Both Model A and Model B continued to project the infectious disease to be controlled even at a lower vaccination rate. At ν=0.5% population per unit t, the total immunized population would reach the level predicted by the HIT at t=131 in both models, and total infections were controlled at 1.22% to 1.24% in Model A and 1.24% to 1.26% in Model B, respectively (Fig. 5E and 5F, Table 3).

At the lowest vaccination rate (ν=0.1% population per unit t), the herd immunity was largely contributed by those immunized through infection. The total immunized population would reach the level predicted by the HIT at t=87, with total infections of 76.33% in the conventional SIR model. Subsequently, total infections continued to increase by 8.09% to reach 84.42% at the end of simulation (Fig. 5G, Table 3). As for Model A, the total immunized population would reach the level predicted by the HIT at t=134, with total infections of 54.08%. At the end of simulation, total infections only increased by another 0.36% to 54.44% in Model A (Fig. 5H, Table 3). In model B, the HIT was reached at t=107, with total infections of 60.68%. At the end of simulation, total infections continued to increase only by another 1.44% in Model B (Fig. 5I, Table 3).

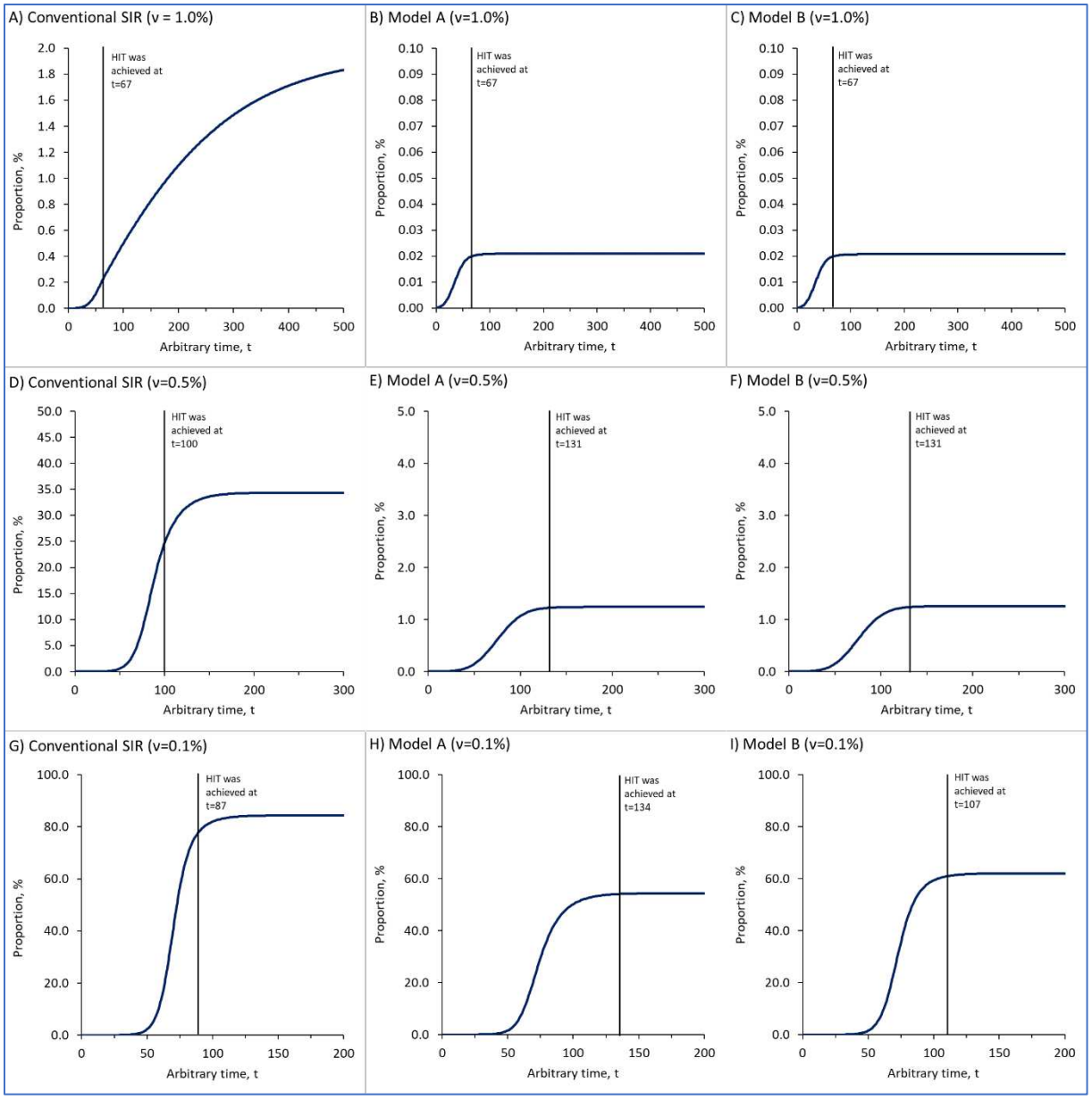

Figure 5: Transmission dynamics of infectious diseases with herd immunity through vaccination
Part A, B and C present transmission dynamics of infectious diseases at vaccination rate, ν=1.0% population per unit t projected by the conventional SIR model, Model A and Model B. The HIT was reached at t=67 in all three models. Part D, E and F present transmission dynamics of infectious diseases at ν=0.5% population per unit t projected by the conventional SIR model, Model A and Model B. The HIT was reached at t=100 in the conventional SIR model, and at t=131 in both Model A and Model B. Part G, H and I present transmission dynamics of infectious disease at ν=0.1% population per unit t projected by the conventional SIR model, Model A and Model B. The HIT was reached at t=87 in the conventional SIR model, at t=134 in Model A, and t=107 in Model B. Times to reach the HIT was marked by vertical lines.

Table 3: Outputs of simulations using the conventional SIR model, Model A and Model B.

Outputs	Conventional SIR model	Model A	Model B
Herd immunity through infection			
HIT was achieved at:	t=134	t=195	t=97
- S(t)	13.1	33.3	26.2
- I(t)	19.2	0	6.5
- Total infections	86.9	66.7	73.8
- R(t)	67.7	66.7	67.3
At the end of simulation (t=200)			
- S(t)	6.0	33.3	24.4
- Total infections	94.0	66.7	75.6
- R(t)	94.0	66.7	75.6
Herd immunity through vaccination			
A) v = 1.0 % population per unit t			
HIT was achieved at:	t=67	t=67	t=67
- S(t)	32.74	32.98	32.98
- I(t)	0.08	0	0
- Total infections	0.26	0.02	0.02
- Total immunized	67.18	67.02	67.02
- Through infection	0.18	0.02	0.02
- Through vaccination	67.00	67.00	67.00
At the end of simulation (t=500)			
- S(t)	31.17	32.98	32.98
- Total infections	1.83	0.02	0.02
- Total immunized	68.82	67.02	67.02
- Through infection	1.82	0.02	0.02
- Through vaccination	67.00	67.00	67.00
B) v = 0.5 % population per unit t			
HIT was achieved at:	t=100	t=131	t=131
- S(t)	26.31	33.28	33.26
- I(t)	6.12	0.04	0.04
- Total infections	24.19	1.22	1.24
- Total immunized	67.58	66.69	66.70
- Through infection	18.08	1.19	1.20
- Through vaccination	49.50	65.50	65.50
At the end of simulation (t=300)			
- S(t)	16.14	33.26	33.24
- Total infections	34.37	1.24	1.26
- Total immunized	83.86	66.74	66.76
- Through infection	34.24	1.24	1.26
- Through vaccination	49.50	65.50	65.50
C) v = 0.1 % population per unit t			
HIT was achieved at:	t=87	t=134	t=107
- S(t)	14.97	32.52	28.62
- I(t)	17.82	0.79	4.29
- Total infections	76.33	54.08	60.68
- Total immunized	67.21	66.70	67.09
- Through infection	58.51	53.30	56.39
- Through vaccination	8.70	13.40	10.70
At the end of simulation (t=200)			
- S(t)	6.90	32.16	27.18
- Total infections	84.42	54.44	62.12
- Total immunized	93.12	67.84	72.82
- Through infection	84.42	54.44	62.12
- Through vaccination	8.70	13.40	10.70

Discussion

Our simulations show that the key to model the transmission dynamics of infectious disease is to allow the transmission rate to decline along with the reducing combined risk of contact infection following recovery. And, this would not alter the early dynamics and basic reproduction number of infectious diseases. However, such modification would lead to very different endings for the same infection as presented in the result section. Infectious diseases modelled by the conventional SIR model appeared to be overly aggressive, and completely impossible to demonstrate control or eradication through herd immunity. This raises a critical concern of using the conventional SIR model or its variants to simulate the ending of the COVID-19 pandemic through herd immunity.

Although Model A successfully demonstrated control and eradication of infectious disease at the level predicted by the HIT, it was not realistic to assume that the transmission rate would decline following infection. Model B provides the framework with a more realistic assumption in modelling the transmission dynamics of infectious diseases with and without vaccination. According to our simulations, the HIT calculated based on the r_0 of infectious diseases is only accurate if we allow the transmission rate to unrealistically decline following infection with or without vaccination. At lower vaccination rates, the total immunized population contributing to herd immunity may consist of largely individuals immunized through infection, which cannot be predicted using the simple threshold theorem anymore. Therefore, further studies are required to investigate and establish the right threshold for estimating the level of herd immunity.

Importantly, our simulations showed that the transmission rate may decline rapidly after a particular time, depending on the population size, contact rate, β and duration of infection. This might help explain the immediate fall of COVID-19 cases in some countries like the United States, United Kingdom and Indonesia, shortly after the rollout of mass and rapid vaccination against the COVID-19 pandemic. Moreover, the newly developed model may provide a better framework for the steady fall of COVID-19 cases in India even without vaccination since September 2020[24]. Many researchers attributed the fall of COVID-19 cases without vaccination in India to herd immunity and younger population demographic. A national serological survey conducted by the Indian Council of Medical Research (ICMR) revealed that up to 21% or 290 million of the adult population in India had developed immunity against the COVID-19 virus[25].

As of this writing, more than 100 million individuals have been infected by the novel coronavirus with a death toll surpassing 2·5 million[24]. At the same time, many countries have started mass and rapid vaccination with the hope to end the COVID-19 pandemic with herd immunity through vaccination. Therefore, the use of the right modelling frameworks for herd immunity becomes critically important and relevant to support post-vaccination public health planning and preparedness against the pandemic.

Conclusion

The key to simulating the transmission dynamics of infectious disease with herd immunity is to allow the transmission rate of infectious disease to decline along with the reducing combined

risk of contact infection following recovery. This can be attained by incorporating the inverse of proportion of recovered individuals into the force of infection of a compartmental model. Further studies are required to establish the right threshold for herd immunity in a randomly mixed population.

References

1. Jones, D. & Helmreich, S. A history of herd immunity. *The Lancet* **396**, 810–811 (2020).
2. Fine, P., Eames, K. & Heymann, D. L. "Herd Immunity": A Rough Guide. *Clin. Infect. Dis.* **52**, 911–916 (2011).
3. Chowell, G., Sattenspiel, L., Bansal, S. & Viboud, C. Mathematical models to characterize early epidemic growth: A review. *Phys. Life Rev.* **18**, 66–97 (2016).
4. Peak, C. M., Childs, L. M., Grad, Y. H. & Buckee, C. O. Comparing nonpharmaceutical interventions for containing emerging epidemics. *Proc. Natl. Acad. Sci.* **114**, 4023–4028 (2017).
5. Mandal, S., Sarkar, R. R. & Sinha, S. Mathematical models of malaria--a review. *Malar. J.* **10**, 202–202 (2011).
6. Law, K. B. *et al.* Tracking the early depleting transmission dynamics of COVID-19 with a time-varying SIR model. *Sci. Rep.* **10**, 21721 (2020).
7. Keeling, M. J. & Danon, L. Mathematical modelling of infectious diseases. *Br. Med. Bull.* **92**, 33–42 (2009).
8. Metcalf, C. J. E., Ferrari, M., Graham, A. L. & Grenfell, B. T. Understanding Herd Immunity. *Trends Immunol.* **36**, 753–755 (2015).
9. Kermack, W. O., McKendrick, A. G. & Walker, G. T. A contribution to the mathematical theory of epidemics. *Proc. R. Soc. Lond. Ser. Contain. Pap. Math. Phys. Character* **115**, 700–721 (1927).
10. Fontanet, A. & Cauchemez, S. COVID-19 herd immunity: where are we? *Nat. Rev. Immunol.* **20**, 583–584 (2020).
11. Kwok, K. O., Lai, F., Wei, W. I., Wong, S. Y. S. & Tang, J. W. T. Herd immunity – estimating the level required to halt the COVID-19 epidemics in affected countries. *J. Infect.* **80**, e32–e33 (2020).
12. Hwang, J., Park, H., Kim, S.-H., Jung, J. & Kim, N. Basic and effective reproduction numbers of COVID-19 cases in South Korea excluding Sincheonji cases. *medRxiv* 2020.03.19.20039347 (2020) doi:10.1101/2020.03.19.20039347.
13. Joseph T, W., Kathy, L. & Gabriel, L. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. *The Lancet* (2020).
14. Zhuang, Z. *et al.* Preliminary estimating the reproduction number of the coronavirus disease (COVID-19) outbreak in Republic of Korea and Italy by 5 March 2020. *Int. J. Infect. Dis.* doi:10.1016/j.ijid.2020.04.044.
15. Zhao, S. *et al.* Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: A data-driven analysis in the early phase of the outbreak. *bioRxiv* 2020.01.23.916395 (2020) doi:10.1101/2020.01.23.916395.
16. Bartsch, S. M. *et al.* Vaccine Efficacy Needed for a COVID-19 Coronavirus Vaccine to Prevent or Stop an Epidemic as the Sole Intervention. *Am. J. Prev. Med.* **59**, 493–503 (2020).

17. Bubar, K. M. *et al.* Model-informed COVID-19 vaccine prioritization strategies by age and serostatus. *Science* eabe6959 (2021) doi:10.1126/science.abe6959.
18. Sandmann, F., Davies, N., Vassall, A., Edmunds, W. J. & Jit, M. The potential health and economic value of SARS-CoV-2 vaccination alongside physical distancing in the UK: transmission model-based future scenario analysis and economic evaluation. *medRxiv* 2020.09.24.20200857 (2020) doi:10.1101/2020.09.24.20200857.
19. Scherer, A. & McLean, A. Mathematical models of vaccination. *Br. Med. Bull.* **62**, 187–199 (2002).
20. Wilson, E. & Worcester, J. The Law of Mass Action in Epidemiology. *Proc. Natl. Acad. Sci. U. S. A.* **31**, 24–34 (1945).
21. Heffernan, J. M., Smith, R. J. & Wahl, L. M. Perspectives on the basic reproductive ratio. *J. R. Soc. Interface* **2**, 281–293 (2005).
22. Siettos, C. I. & Russo, L. Mathematical modeling of infectious disease dynamics. *Virulence* **4**, 295–306 (2013).
23. Dietz K. Transmission and control of arbovirus diseases. In: Ludwig D, Cooke KL, eds. Epidemiology. Pheladelphia PA: Society for Industrial and Applied Mathematics, 1975: 104-21.
24. *Johns Hopkins University Coronavirus Resources Center*. https://coronavirus.jhu.edu/.
25. ICMR sero survey: One in five Indians exposed to Covid-19. *BBC News* (2021).

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Competing interests
The authors declare no competing interests.

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Author Contributions
K.B.L and K.M.P conceived and planned the study.
K.B.L contributed to the design of the compartmental model and simulation.
K.M.P, H.S and N.H.A supervised the implementation of the study.
Data analysis and graphics were done by K.B.L.
All authors contributed to the interpretation of the findings and writing of article and approved the final version for publication.

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561
562 **Ethics requirement**
563 The study was registered with National Medical Research Register. No ethics approval was
564 required.

Figures

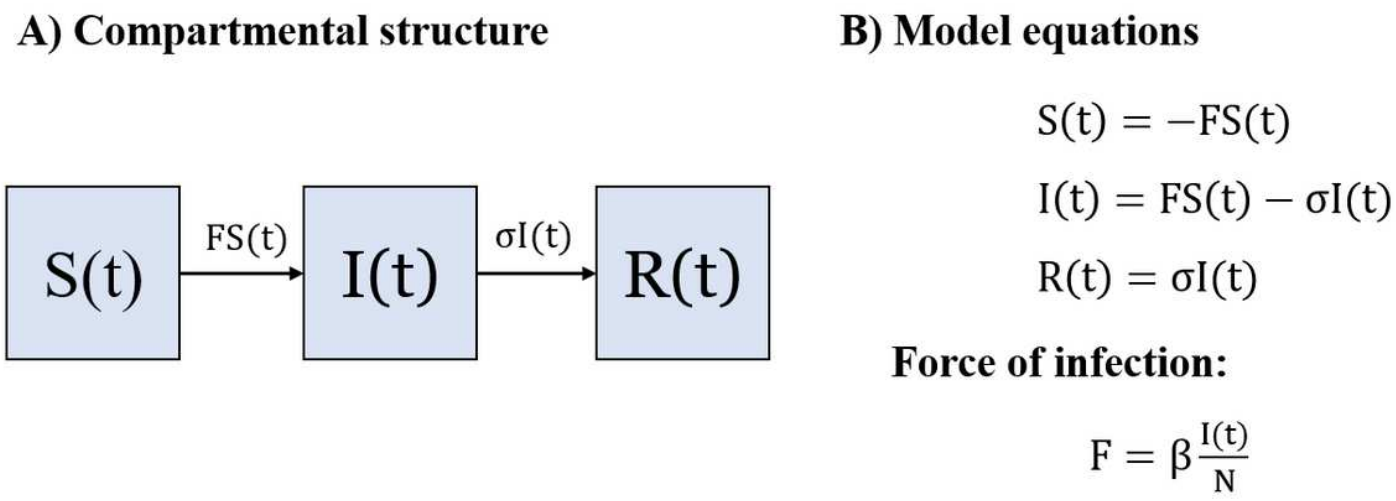

Figure 1

The compartmental structure and model equations of Kermack & Mckendrick's SIR model.

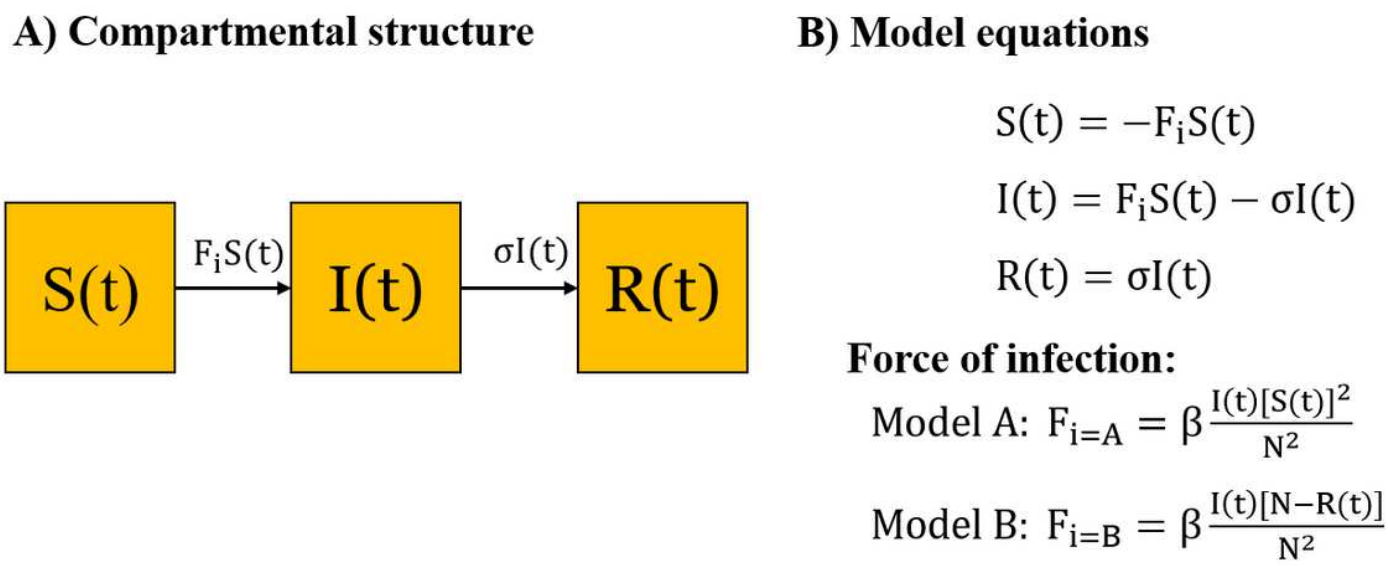

Figure 2

The compartmental structure and model equations of the newly developed Model A and Model B.

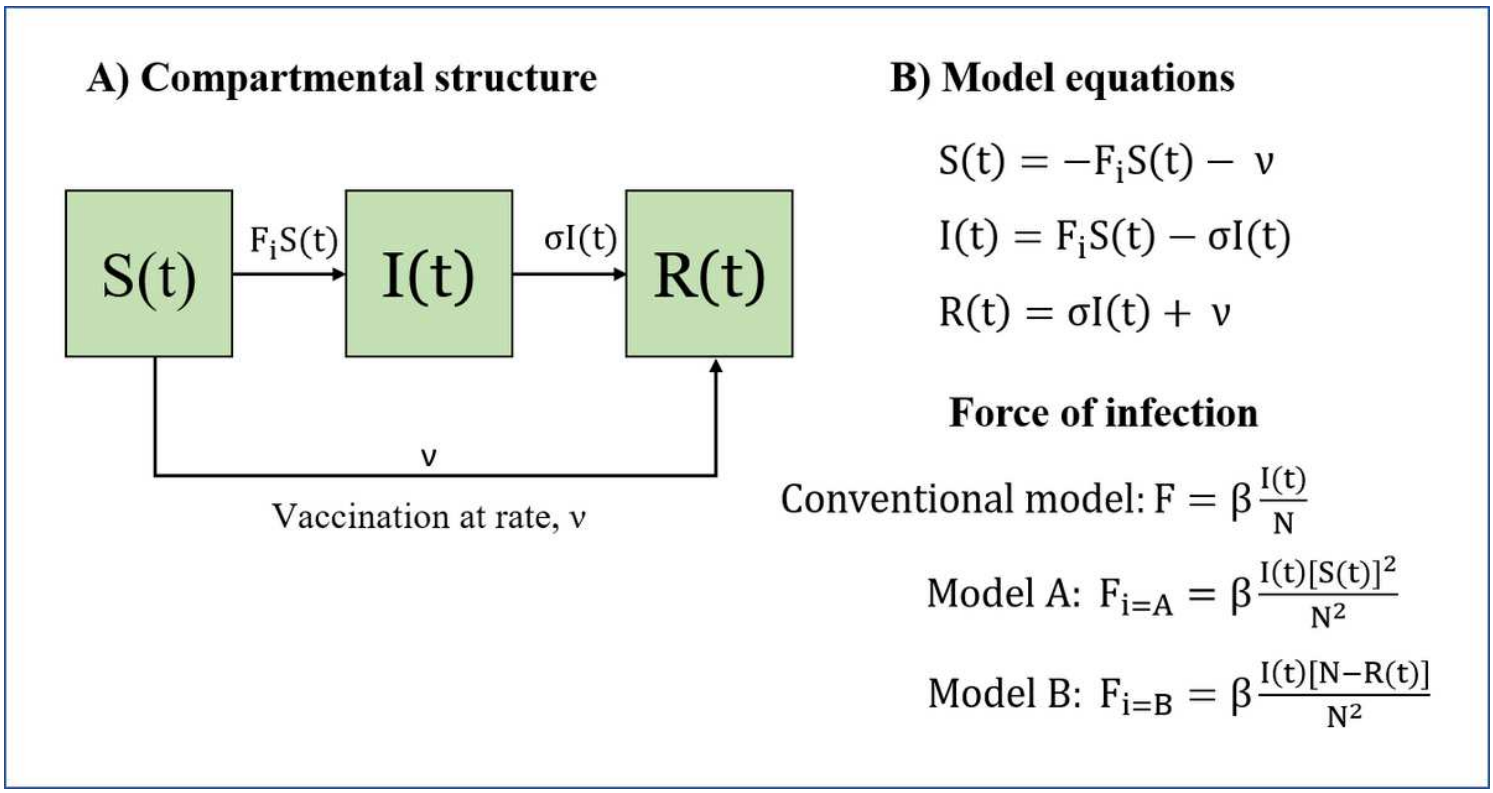

Figure 3

The compartmental structure and model equations of vaccine models modified using the conventional SIR model, Model A and Model B.

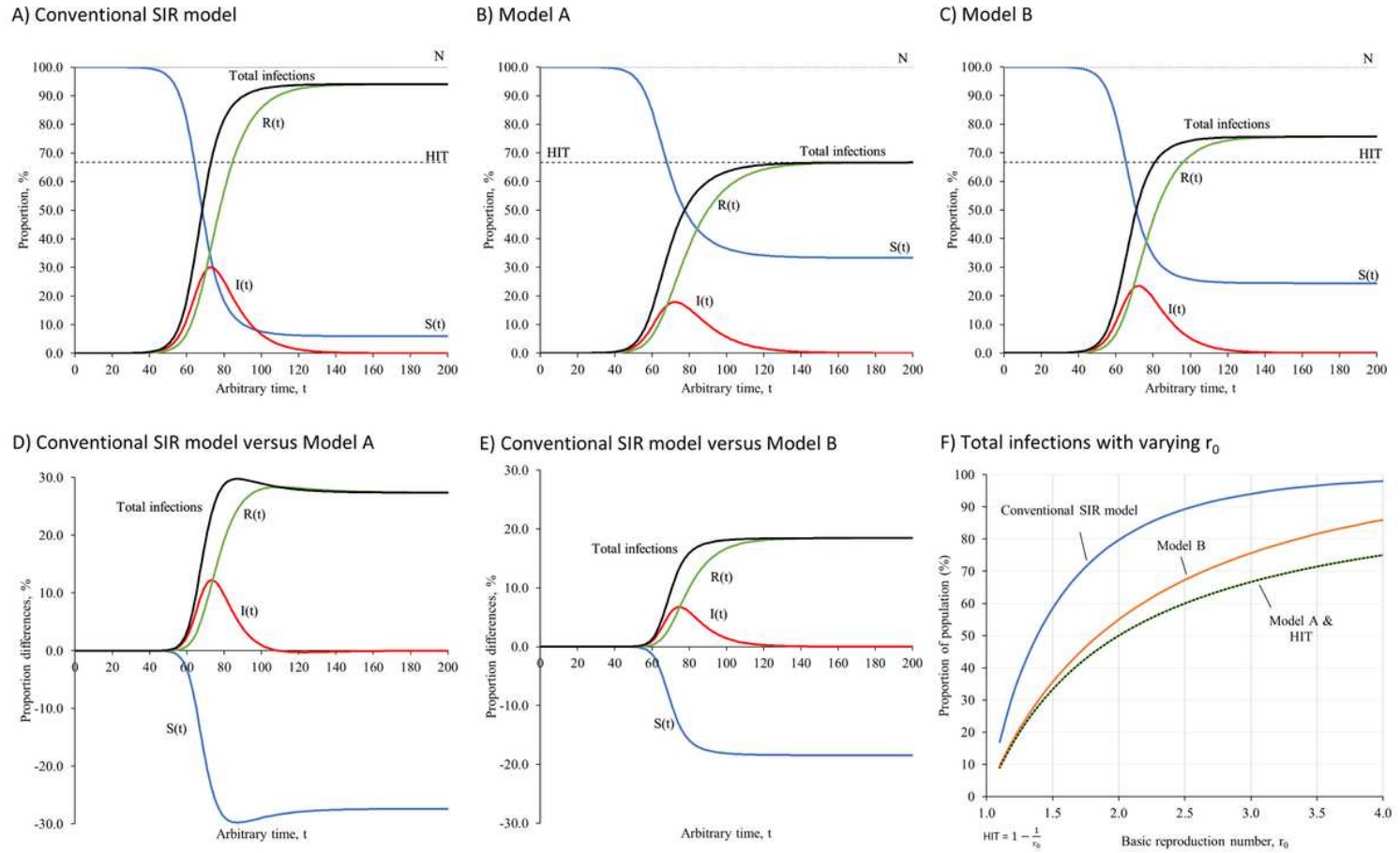

Figure 4

Transmission dynamics of infectious diseases with herd immunity through infection Part A, B and C presents transmission dynamics of infectious diseases with herd immunity through infection simulated by the conventional SIR model, Model A and Model B. Part D and E presents proportion differences between the conventional SIR model and Model A and between the conventional SIR mode and Model B. Part F presents total infections generated by the conventional SIR model, Model A and Model B with varying r0.

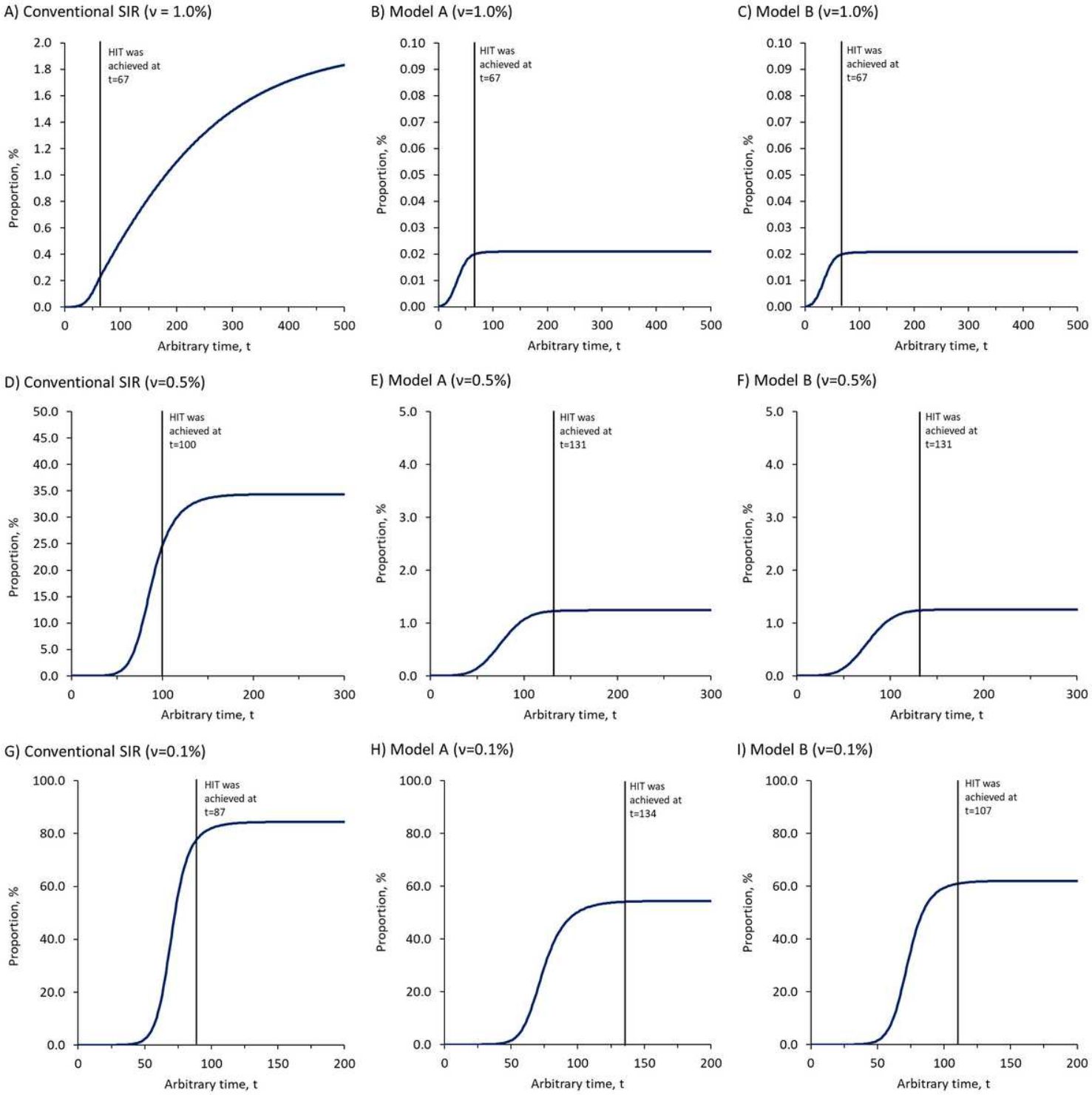

Figure 5

Transmission dynamics of infectious diseases with herd immunity through vaccination Part A, B and C present transmission dynamics of infectious diseases at vaccination rate, v=1.0% population per unit t projected by the conventional SIR model, Model A and Model B. The HIT was reached at t=67 in all three models. Part D, E and F present transmission dynamics of infectious diseases at v=0.5% population per unit t projected by the conventional SIR model, Model A and Model B. The HIT was reached at t=100 in the conventional SIR model, and at t=131 in both Model A and Model B. Part G, H and I present transmission dynamics of infectious disease at v=0.1% population per unit t projected by the conventional SIR model, Model A and Model B. The HIT was reached at t=87 in the conventional SIR model, at t=134 in Model A, and t=107 in Model B. Times to reach the HIT was marked by vertical lines.