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A Mathematical Model of the Diphtheria Infection

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Abstract

This work considers the mathematical model of diphtheria disease. A five compartmental model was formulated to group the human population into susceptible (S), exposed (E), infectious (I), treatment (T) and recovered (R). The basic reproduction number (R_0) of the model was established and was subsequently used to show that the formulated model is locally asymptotically stable ($R_0 < 1$). The model was further analyzed with the aid of graphs, and the results show that despite the efficacy of diphtheria vaccine in the prevention of contracting the disease, the most important factor in the Nigeria case after the breakout of the disease is case detection. The more cases detected, the easier it would be to curb the infection.

Keywords: diphtheria infection, mathematical model, case detection, vaccine, reproduction number.

1. Introduction

Diphtheria, a highly contagious but vaccine preventable bacterial infection is caused by *Corynebacterium diphtheria* [2, 4, 5]. This infection can be asymptomatic which may prevent immediate detection. It primarily infects the throat and nose (respiratory diphtheria) by the development of gray white patch in the throat, which could in turn block the airway [3]. Cutaneous diphtheria is another rare type of diphtheria infection. This causes pain, redness and swelling, just like other bacterial skin infections [19]. Other body sites that could be affected are the eyes, ears and genitals [20].

Diphtheria, an infection with 2-5 days incubation period is transmitted through respiratory droplets, physical contact, contagious cutaneous diphtheria lesions, contaminated clothing and objects [4]. When diphtheria is left unattended to, it could lead to serious breathing problems as well as heart and nerve damage [19]. The risk factors of the infection include; non/partial vaccination, damaged health infrastructure and health services, conflict hit zones and overcrowding. It is worth mentioning that it affects all age groups [7, 17].

Since the first description of the disease in the 5th century BC by Hippocrates [2], the first significant reported case of the infection in Nigeria was in 2011, when it ravaged rural areas of Borno State [4, 5]. In December, 2022, the Nigeria Centre for Disease Control and Prevention (NCDC) got notified of suspected cases of diphtheria disease outbreak in Kano and Lagos states. As at 11th February, 2024, Nigeria has already recorded 27,078 suspected cases, out of which 16,603 cases were confirmed. These figures put the confirmed cases to be 61.3% of the suspected cases, while the total deaths recorded stand at 650 [16]. According to the WHO, the 2024 suspected cases as at 11th February, 2024 is already 3,119 with 2,465 confirmed cases and 33 deaths [16]. That

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puts the confirmed cases to over 79%. If not promptly treated, case fatality rate (CFR) could be up to 10% [7, 17]. In fact, Nigeria had 21.4% CFR when the 2011 Borno outbreak occurred, with 98 cases, out of which 63 were children with 42.9% CFR among 0-4 years old kids [6].

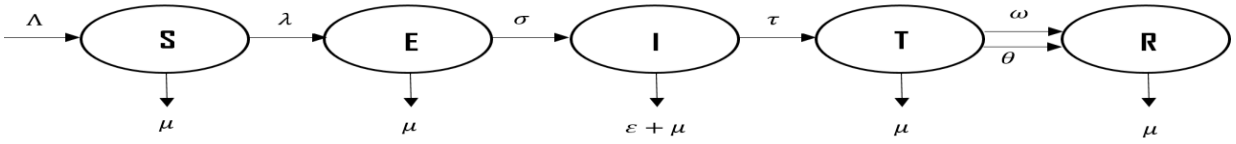
Diphtheria infection can be diagnosed in the laboratory by taking at least two specimens from the pharynx, nasopharynx or nasal space. It can as well be done by carrying out PCR tests to query the presence of diphtheria toxin [7, 18].

Mathematical modelling of diseases has been an old tool in analyzing and predicting the behavior of diseases. Different authors like [10-15], have at different times used it, and the results have been useful to health practitioners and policy makers. A mathematical model of diphtheria infection is formulated in this work, and it is partitioned into five parts, inclusive of this introduction. Others are the model formulation, model analysis, discussion of results and conclusion. With diphtheria vaccine in place, the research aims to check why the infection still affects a huge population and what actually causes its re-emergence.

2. Model Formulation and Analysis

2.1 The Model

This research presents the mathematical model of diphtheria infection. Human population are subdivided into five groups, depending on their health status (with reference to diphtheria infection). The first category of people considered are the susceptible class designated as S. This is the group of individuals that reside in the location where there is outbreak of diphtheria infection. People are recruited into this class at the rate Λ. The next group of individuals in this categorization fall in the exposed class E. These are the set of individuals who have got exposed to the diphtheria infection. They have contracted the infection but not yet showing the symptoms of diphtheria infection. Individuals from the susceptible class get recruited into this class at the rate λ. λ defined in equation (2) is the disease transmission rate. Individuals from the exposed class move to the infectious class I at the rate σ. At this stage, individuals who contract the diphtheria infection have already manifested full symptoms of diphtheria and are already transmitting the infection to unsuspecting individuals. When these set of individuals present themselves for treatment at health centres, they move to the treatment compartment T at the rate τ. When these set of individuals decide to place themselves on self-medication, it could be counterproductive as they will most likely be on wrong medication. This is one of the reasons that promote the persistence of the disease as not all infected persons are captured for treatment. While getting treatment, individuals can move to the recovered class R at the rate ω, representing the natural/inexplicable recovery or due to treatment at the rate θ. Death could occur naturally at the rate μ or due to diphtheria infection at the rate ε. It is worthy to note that the population is homogeneously mixed.



$$\frac{dS}{dt} = \Lambda - (\lambda + \mu)S$$

$$\frac{dE}{dt} = \lambda S - (\sigma + \mu)E$$

$$\frac{dI}{dt} = \sigma E - (\tau + \varepsilon + \mu)I \qquad (1) \qquad\qquad \lambda = \frac{\beta(\phi E + I)}{N} \qquad (2)$$

$\frac{dT}{dt} = \tau I - (\omega + \theta + \mu)T$

$\frac{dR}{dt} = (\omega + \theta)T - \mu R$

2.2 Positivity of the model

Lemma 2.1: *Suppose the initial conditions for the model* (1) *is* $S(0) \geq 0, E(0) \geq 0, I(0) \geq 0, T(0) \geq 0$ *and* $R(0) \geq 0$, *then the solutions* (S, E, I, T, R) *of the model with positive initial conditions remain positive for all time* $t > 0$.

2.3 Analysis

2.3.1 Basic Reproduction Number (R_0)

The basic reproduction number of a disease is the number of secondary infections from a primarily recorded one. For an infection to be contained, R_0 must be kept less than one ($R_0 < 1$). $R_0 > 1$ implies the recorded infection could turn into an epidemic. The basic reproduction (R_0) is established using the next generation matrix as discussed in [8, 9] and used in [10-12]. Following the notations used in [8, 9], then $\mathcal{F}$ and v matrices for the new infection terms and the remaining transition terms are respectively given by equation (4). The method defines the R_0 as equation (3) below, where ρ (called the spectra radius) means the dominant eigenvalue of the matrix.

$$R_0 = \rho(FV^{-1}) \quad (3)$$

F and V are as defined in (5) below and V^{-1} also established in the same equation

$$\mathcal{F} = \begin{bmatrix} \lambda S \\ 0 \end{bmatrix}, v = \begin{bmatrix} (\sigma + \mu)E \\ (\tau + \varepsilon + \mu)I - \sigma E \end{bmatrix} \quad (4)$$

$$F = \begin{bmatrix} \beta\phi & \beta \\ 0 & 0 \end{bmatrix}, \qquad V = \begin{bmatrix} \sigma + \mu & 0 \\ -\sigma & \tau + \varepsilon + \mu \end{bmatrix}, \qquad V^{-1} = \frac{1}{(\sigma + \mu)(\tau + \varepsilon + \mu)} \begin{bmatrix} \tau + \varepsilon + \mu & 0 \\ \sigma & \sigma + \mu \end{bmatrix} \quad (5)$$

$$\Longrightarrow R_0 = \frac{1}{(\sigma + \mu)(\tau + \varepsilon + \mu)} \begin{bmatrix} \beta\phi & \beta \\ 0 & 0 \end{bmatrix} \begin{bmatrix} \tau + \varepsilon + \mu & 0 \\ \sigma & \sigma + \mu \end{bmatrix}$$

$$\Longrightarrow R_0 = \frac{\beta[\phi(\tau + \varepsilon + \mu) + \sigma]}{(\sigma + \mu)(\tau + \varepsilon + \mu)} \quad (6)$$

2.3.2 Stability Analysis

Lemma 3.2.1 *The DFE (disease free equilibrium) of the model (1) is locally asymptotically stable (LAS) if* $R_0 < 1$ *and unstable otherwise.*

Proof: The DFE of the model is gotten by setting the left hand side of equation (1) to zero and subsequently solving for the variables S, E, I, T and R. This is gotten to be $\{S, E, I, T, R\} = \{\frac{\Lambda}{\mu}, 0,0,0,0\}$. Let the dynamics in each compartment be represented as f_1, f_2, f_3, f_4 and f_5 respectively, then the Jacobian matrix of the equation (1) is as presented in equation (6) below.

Upon the evaluation of equation (6) at the DFE and subsequently establishing its eigenvalues to be $\eta_1 = -\mu$, $\eta_2 = -\mu, \eta_3 = -(\omega + \theta + \mu)$, the remaining 2 eigenvalues are found using equation (7)

$$\begin{bmatrix} \frac{\partial f_1}{\partial S} & \frac{\partial f_1}{\partial E} & \frac{\partial f_1}{\partial I} & \frac{\partial f_1}{\partial T} & \frac{\partial f_1}{\partial R} \\ \frac{\partial f_2}{\partial S} & \frac{\partial f_2}{\partial E} & \frac{\partial f_2}{\partial I} & \frac{\partial f_2}{\partial T} & \frac{\partial f_2}{\partial R} \\ \frac{\partial f_3}{\partial S} & \frac{\partial f_3}{\partial E} & \frac{\partial f_3}{\partial I} & \frac{\partial f_3}{\partial T} & \frac{\partial f_3}{\partial R} \\ \frac{\partial f_4}{\partial S} & \frac{\partial f_4}{\partial E} & \frac{\partial f_4}{\partial I} & \frac{\partial f_4}{\partial T} & \frac{\partial f_4}{\partial R} \\ \frac{\partial f_5}{\partial S} & \frac{\partial f_5}{\partial E} & \frac{\partial f_5}{\partial I} & \frac{\partial f_5}{\partial T} & \frac{\partial f_5}{\partial R} \end{bmatrix} = \begin{bmatrix} -(\lambda+\mu) & \beta\phi & \beta & 0 & 0 \\ \lambda & \beta\phi-(\sigma+\mu) & \beta & 0 & 0 \\ 0 & \sigma & -(\tau+\varepsilon+\mu) & 0 & 0 \\ 0 & 0 & \tau & -(\omega+\theta+\mu) & 0 \\ 0 & 0 & 0 & (\omega+\theta) & -\mu \end{bmatrix} \quad (6)$$

$$\begin{bmatrix} \beta\phi-(\sigma+\mu)-\eta & \beta \\ \sigma & -(\tau+\varepsilon+\mu)-\eta \end{bmatrix} = 0$$

$$\eta^2 + [(\tau+\varepsilon+\mu)+(\sigma+\mu)-\beta\phi]\eta + (\tau+\varepsilon+\mu)(\sigma+\mu) - \beta[\phi(\tau+\varepsilon+\mu)+\sigma] = 0 \quad (7)$$

$$\Longrightarrow \eta^2 + [(\tau+\varepsilon+\mu)+(\sigma+\mu)-\beta\phi]\eta + (\sigma+\mu)(\tau+\varepsilon+\mu)\left(1-\frac{\beta[\phi(\tau+\varepsilon+\mu)+\sigma]}{(\sigma+\mu)(\tau+\varepsilon+\mu)}\right) = 0$$

$$\Longrightarrow \eta^2 + [(\tau+\varepsilon+\mu)+(\sigma+\mu)-\beta\phi]\eta + (\sigma+\mu)(\tau+\varepsilon+\mu)(1-R_0) = 0$$

$$\therefore \eta_{4,5} = \frac{-[(\tau+\varepsilon+\mu)+(\sigma+\mu)-\beta\phi] \pm \sqrt{[(\tau+\varepsilon+\mu)+(\sigma+\mu)-\beta\phi]^2 - 4(\sigma+\mu)(\tau+\varepsilon+\mu)(1-R_0)}}{2}$$

$$\Longrightarrow \eta_{4,5} < 0 \Leftrightarrow R_0 < 1$$

The stability of the model is guaranteed when all the associated eigenvalues are negative (< 0). $R_0 > 1$ implies the disease cannot be contained but rather becomes an epidemic.

3. Results and Discussion

The numerical results of the model (1) are presented in this section. The values used in the computation with their sources are as presented in Table 4.1 while the presented graphs were plotted using MATLAB R2020b. The graphical simulation was done over a 10 week period with an arbitrarily chosen initial population of $\{S, E, I, T, R\} = \{345, 234, 122, 10, 0\}$. Figures 4.1 (a) and 4.1 (b) present the population in each compartments over this 10 week period. There is tremendous increment in each population, perhaps, due to the recruitment rate Λ. The Figure 4.1 (a) shows the dynamics of each population when the case detection rate (τ) is 20%. The susceptible class (S) stands at 86,860, exposed (E), 134,700, infected (I), 46,910, treatment (T), 6204 and recovered (R), 10,050.

When the surveillance is increased and the case detection rate is raised to 80%, the susceptible class (S) increases by 7.5%, the exposed (E) decreases by 3.8%, the infectious (I) reduces by 43.4%, the treatment class (T) increases by 126% while the recovered class increases by 130%. This shows the great impact case detection has on curbing the spread of diphtheria infection. The increment in the susceptible class explains that lesser number of people contract the infection after the bar of the case detection has been increased.

Figures 4.2 to 4.5 give the analysis of the effect of both the vaccine efficacy (ϕ) and case detection (τ). Figures (a) in this category present the results when only 3% of the exposed class contribute to the disease incidence. This is due to the fact that diphtheria vaccine efficacy stands at 97% [2]. Figures (b) in this category present the results when 100% of the exposed class contribute to the disease incidence. This could be due to the fact that

vaccination coverage is some Nigerian states is less than 20% ($< 20\%$) [1]. This shows there will be some communities with 0% vaccination coverage.

The Figures in 4.2 present the dynamic of the exposed population. It shows that there is almost no effect of the case detection on disease management if the whole of the exposed class contribute to the disease incidence. On the other hand, with 3% of the exposed population contributing to the disease incidence and 100% case detection, the population reduces by $8.8.\%$ compared to 100% of the exposed contributing to the disease incidence.

As for the infected population, this is presented by Figure 4.3. In both Figures (a and b), case detection play significant role as the percentage difference between 100% case detection and 0% (when only 3% of the exposed individuals contribute to the disease incidence) is 168%, i.e., 38,710 cases were averted. When all the exposed contribute to the disease incidence, and 100% case detection achieved, 38,460 cases were averted. This represents about the same percentage of cases averted with 3% disease incidence contributory percentage compared to 0% detection rate.

When the treatment compartment is considered, 15,230 more persons were captured for the 3% disease incidence contributory percentage. This means that $152{,}300\%$ more persons were captured while the 100% disease incidence contributory percentage gives the opportunity to capture 16,810 more persons. This is due to the fact that more persons contract the infection when ϕ is 1 (100% disease incidence contributory percentage). In both cases, the maximum persons captured for treatment when case detection is 0% is 10, which is the value of the initial population defined.

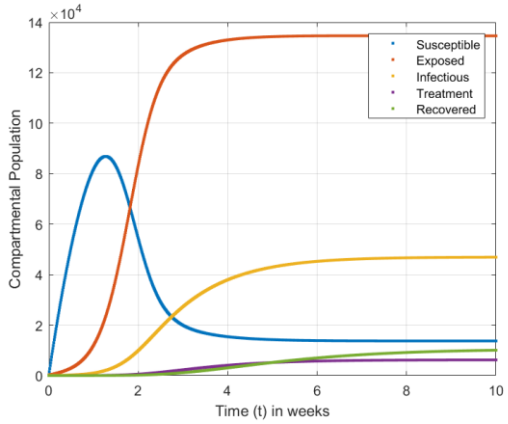
When there is 0% case detection in both cases of $\phi = 0.03$ and $\phi = 1$, the maximum recovered population is 3. This is due to the naturally inexplicable recovery rate, ω. 25,127 and 27,867 more persons recover in both cases of 0.03% and 100% when there is 100% case detection.

Table 4.1: Table of values

S/No	Parameter	Meaning	Value	Source
1	Λ	Recruitment rate	123456	Assumed
2	β	Infection rate	0.35×100	Assumed
3	ϕ	Non-effectiveness of vaccine	0.03	[2]
4	σ	Progression rate from E to I	0.3	modified
5	τ	Case detection rate	80%	Assumed
6	ω	Natural recovery rate	20%	Assumed
7	θ	Treatment induced recovery	80%	Assumed
8	μ	Natural death rate	0.1	Assumed

4. SUMMARY

This research presents a mathematical model of diphtheria infection. This is coming after the resurgence of the disease in late 2022 in some parts of Nigeria. A five-compartment model is formulated and used in explaining the dynamics of the infection. It is found that despite the efficacy of the diphtheria vaccine, which stands at about 97%, the most effective way of combatting the infection is through efficient case detection. Without reasonable case detection rate, the impact of the vaccine would not be felt.



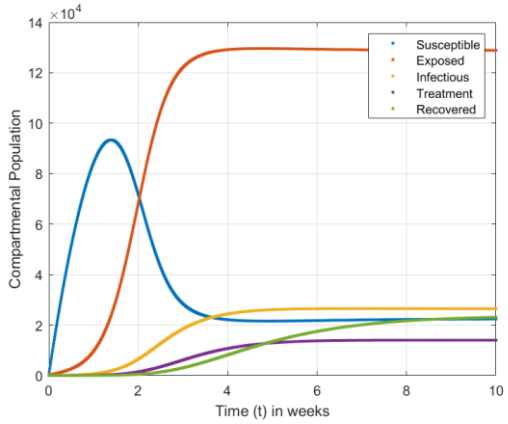
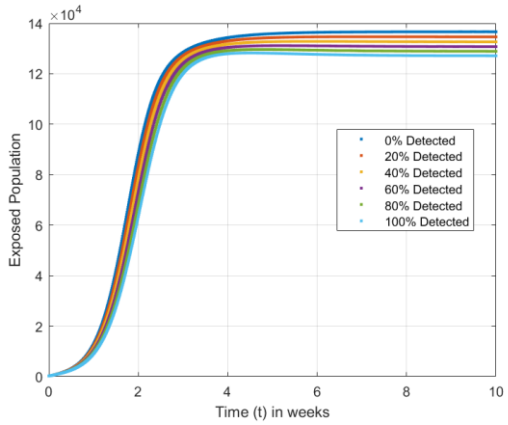


Figure 4.1: (a) Compartmental Population ($\tau = 0.2$) (b) Compartmental Population ($\tau = 0.8$)



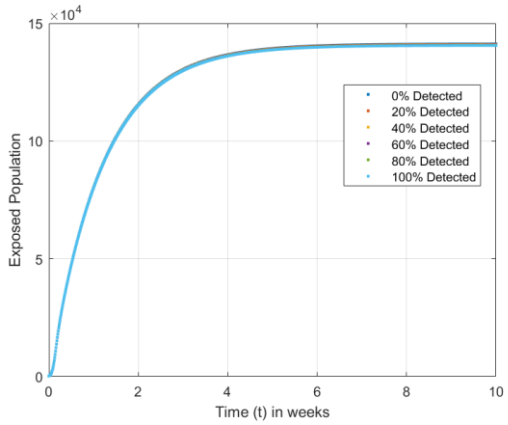
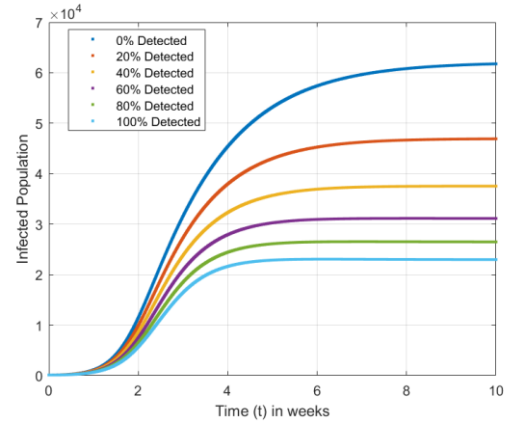


Figure 4.2: (a) Exposed Population ($\phi = 0.03, \tau = 1$) (b) Exposed Population ($\phi = 1, \tau = 1$)



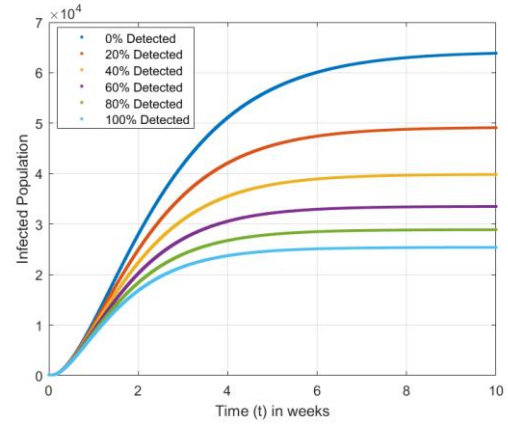
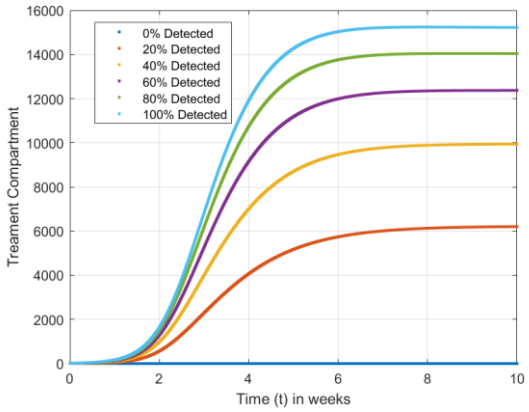


Figure 4.3: (a) Infected Population ($\phi = 0.03, \tau = 1$) (b) Infected Population ($\phi = 1, \tau = 1$)



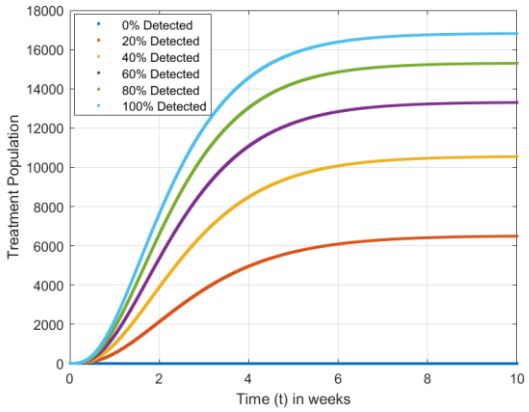
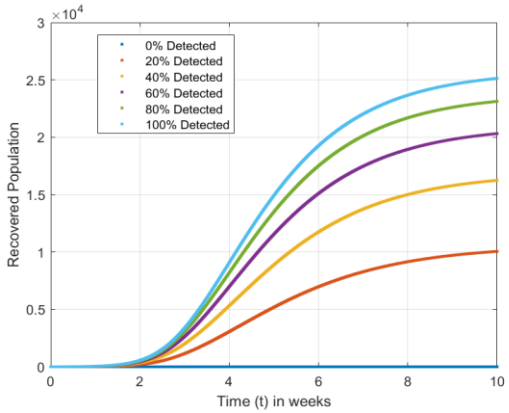


Figure 4.4: (a) Treatment Compartment ($\phi = 0.03, \tau = 1$) (b) Treatment Compartment ($\phi = 1, \tau = 1$)



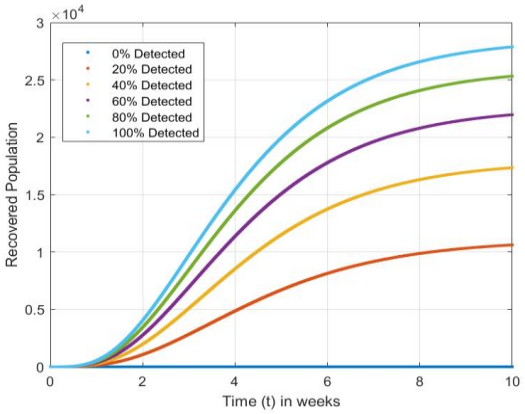


Figure 4.5: (a) Recovered Population ($\phi = 0.03, \tau = 1$) (b) Recovered Population ($\phi = 1, \tau = 1$)

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