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Cover Page Footnote

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Age-Structured and Vaccination Models of Devil Facial Tumor Disease

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Abstract

Tasmanian devil populations have been devastated by devil facial tumor disease (DFTD) since its first appearance in 1996. The average lifespan of a devil has decreased from six years to three years. We present an age-structured model to represent how the disease has affected the age and breeding structures of the population. We show that with the recent increase in the breeding of juvenile devils, the overall devil population will increase but not nearly to pre-DFTD levels. The basic reproductive number may be increased with the influx of young breeding devils. In addition, our model shows that the release of nearly 100 captive-bred, vaccinated devils into infected, wild populations may help eliminate the disease and hence enable the population's recovery. Specifically, we demonstrate that with this release of captive-bred, vaccinated devils the basic reproductive number is decreased to below one.

Keywords: Tasmanian devil, DFTD, epidemiology, vaccination, Devil facial tumor disease

1 Introduction

Tasmanian devils (*Sarcophilus harrisii*) have been battling the transmissible cancer, devil facial tumor disease (DFTD) since the disease's appearance in 1996 [1]. This disease is characterized by large cancerous tumors that form in the cranial region and is one of very few known transmissible cancers [2, 3]. Because of this disease, the overall devil population has decreased by over 90% in some local regions [1, 4]. The disease thus far has a 100% mortality rate, with the cause of death often being starvation due to throat blockage [5]. Devils have a lifespan of three years in areas where DFTD is present, which is down from their normal lifespan of six years [1, 6].

DFTD has been so devastating to devil populations because of their low genetic diversity. The major histocompatibility complex does not recognize the invading cancerous cells as foreign bodies [5, 7]. DFTD is believed to be transmitted by a devil biting the tumor of another devil [8]. The onset of the disease has caused a variety of changes to the devil populations, including an increased reproductive window from one month to two months, infected mothers giving birth to a higher number of females than males, and an increased number of breeding juvenile devils [9]. Breeding occurs typically in females between the ages of two years and four years and in males between the ages of two years and five years, with a small num-

ber of female and male one-year-olds (juvenile). Females can support a maximum of four surviving young per litter [1, 6]. The depletion of adult devils has decreased the competition for resources and hence enabled more juvenile devils to reach breeding size sooner [9]. Previous age-structured models did not incorporate the increased breeding by younger female devils in DFTD affected areas [10]. Our model accounts for this increased breeding of juvenile devils and supports Beeton's conclusion that this increase will not be sufficient to regain pre-DFTD population numbers [10].

Several conservation strategies have been considered to help reduce the spread of DFTD in wild populations and hence increase overall devil populations. Captive breeding is expanding in Australia and other countries, and captive-bred devils have been successfully released into the wild in populations in which DFTD is not present [11]. Selective culling of infected devils has been considered but previous models found this strategy would not be an effective means of disease control for DFTD [10, 12]. Due to no documented vertical transmission of the disease, fertility control has not been considered. Recently, there has been promising advances in devil immune system understanding and research in vaccine development, which may eventually allow for disease prevention [13]. While vaccination of wild devils is possible, we consider the more immediate potential strategy of releasing captive-bred, vaccinated devils into wild populations affected with DFTD. By showing that the basic reproductive number can be reduced to less than one by releasing vaccinated, captive-bred devils, our model supports the assertion that releas-

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ing these devils will help inhibit the disease's ability to continue ravaging local populations and enable declining populations to rebound.

2 Age-Structured Model

To determine the minimum percentage of breeding, juvenile females needed to stabilize the population, we use a Susceptible-Exposed-Infected (SEI) model with no recovered class included due to the 100% mortality rate of the disease [4]. Every devil that is born is susceptible because there is no documented vertical transmission of the disease [4]. Exposed devils are those that have had a contact event that caused disease contraction, but have not yet shown symptoms. The infected classes are those devils that have visible tumors. Devils enter the general interactive population between nine and twelve months of age because devils under one year old have minimal contact with adults [4]; thus, our model neither considers devils less than one year old as part of the interactive population nor includes exposed and infected classes for devils that are less than one year old. Let S_0 denote the number of susceptible newborns, which includes the devils in the age interval $[0, 1)$ years. For $i = 1, 2, 3$, we denote by S_i , E_i , and I_i , the numbers of susceptible, exposed, and infected devils in the age interval $[i, i + 1)$, respectively. We also let $N_i = S_i + E_i + I_i$, for $i = 1, 2, 3$, $P = N_1 + N_2 + N_3$, and $I = I_1 + I_2 + I_3$. The disease prevalence term is simply $\frac{I}{P}$.

Devils enter the population through the newborn S_0 class at a rate of

$$\sum_{i=1}^3 yqr_i N_i,$$

where y is the average number of surviving young per mother, q is the fraction of females, and r_i the percentage of reproducing females in age class $i = 1, 2, 3$. Note that r_1 is less than r_2 and r_3 . Devils leave the S_0 class either by death at a rate of d_{s_0} or by maturing to the S_1 class. Young devils do not interact with devils outside of the den and cannot contract DFTD from their mother, so the infection rate of devils in the youngest age class is zero. For $i = 1, 2, 3$, devils enter the class S_i from the class S_{i-1} by maturation and leave the S_i class by natural death at a rate of d_{s_i} , by frequency-dependent exposure to the disease with a transmission rate k , or, for $i = 1, 2$ only, by maturation to the next susceptible age class S_{i+1} . As juvenile devils have been observed to have fewer interactions than adults, they have a reduced transmission rate of bk where $0 < b < 1$ for one-year-old devils [10]. Prior to the introduction of DFTD, the average lifespan of a devil was six years, but now, very few devils over three years old have been found where the disease has emerged [6, 9]. Therefore, the classes S_3 , E_3 and I_3 are further

expanded to include devils that are at least three years old, and devils in the S_3 age class leave not by maturation but rather by natural death or by becoming infected.

Devils enter the exposed classes by becoming infected and leave the classes by natural death (assumed to be at the same rate as for susceptible devils) or by showing symptoms after a latency period L . As the latency period has been found to be six to twelve months [15], we assume exposed devils enter the infected class before maturing to the next exposed age class.

For $i = 1, 2, 3$, devils enter the infected class I_i at a rate of E_i/L , following the latency period, and leave due to natural death (at the same rate as for susceptible devils) or to death due to the infection at a rate of d_I .

Assuming that the duration of the disease from exposure to death is approximately one year, infected individuals do not mature to the next age class. We do not consider immigration and emigration of devils. The model we have just described is given by System (1) below:

$$\begin{aligned} S'_0(t) &= yq \left(\sum_{i=1}^3 r_i N_i \right) \left(1 - \frac{P}{K} \right) - d_{s_0} S_0 - S_0 \\ S'_1(t) &= S_0 - d_{s_1} S_1 - bk S_1 \frac{I}{P} - S_1 \\ S'_2(t) &= S_1 - d_{s_2} S_2 - k S_2 \frac{I}{P} - S_2 \\ S'_3(t) &= S_2 - d_{s_3} S_3 - k S_3 \frac{I}{P} \\ E'_1(t) &= bk S_1 \frac{I}{P} - d_{s_1} E_1 - \frac{1}{L} E_1 \\ E'_2(t) &= k S_2 \frac{I}{P} - d_{s_2} E_2 - \frac{1}{L} E_2 \\ E'_3(t) &= k S_3 \frac{I}{P} - d_{s_3} E_3 - \frac{1}{L} E_3 \\ I'_1(t) &= \frac{1}{L} E_1 - d_{s_1} I_1 - d_I I_1 \\ I'_2(t) &= \frac{1}{L} E_2 - d_{s_2} I_2 - d_I I_2 \\ I'_3(t) &= \frac{1}{L} E_3 - d_{s_3} I_3 - d_I I_3. \end{aligned} \tag{1}$$

2.1 Equilibrium Values and Basic Reproductive Number

We consider all non-negative, real equilibrium points of System (1) with parameter values from Table 1. We find an extinction equilibrium when the devils have gone extinct and an unstable disease free equilibrium point of $S_0^* = 28.727$, $S_1^* = 19.2758$, $S_2^* = 14.8275$, $S_3^* = 11.1485$ for a total population around 74 devils, a reduction of 57.22% from the initial conditions population. Baby devils are reduced by 62.33%, and juveniles are reduced by 68.33%. Pre-disease, for this local population, baby and juvenile devils made up 79.2% of the population, and

Table 1: Parameter Values.

Parameter	Value	Units	Description	Citation
y	3.42	per (adults*year)	Average number of devils per litter	[9]
r_1	0.4	—	Fraction of one-year-old females reproducing	[9]
r_2	0.9	—	Fraction of two-year-old females reproducing	[6]
r_3	0.9	—	Fraction of three-year-old females reproducing	[6]
q	0.50	—	Fraction of devils that are female	[2]
K	217	devils	Carrying capacity	[2]
d_{S_0}	0.22	per year	Baby devil death rate	[2]
d_{S_1}	0.49	per year	One-year-old death rate	[2]
d_{S_2}	0.30	per year	Two-year-old death rate	[2, 9]
d_{S_3}	0.33	per year	Three-year-old death rate	[2, 9]
d_{S_4}	0.40	per year	Four-year-old death rate	[6]
d_{S_5}	0.836	per year	Five-year-old death rate	[6]
d_{S_6}	1	per year	Six-year-old death rate	[6]
d_I	1.28	per year	Infected death rate	[2]
k	10	transmission*contacts/year	Contacts per year	[9, 14–18]
b	0.602	—	Transmission reduction	[10]
L	0.75	years	Latency period	[15]
β	2	adults per year	Captive-bred vaccinated devils released to wild	[13]
σ	0.25	—	Vaccine failure percent	[13]

Figure 1: Age-structure model equilibrium points varying by percent of one-year-old devils reproducing (r_1).

post-disease those same age classes make up 65.75% of the population. We show in Figure 1 how these equilibrium values vary as the percent of one-year-old devils reproducing increases.

A disease's ability to invade a population is based on the basic reproductive number R_0 , which gives the average number of secondary infections from one infected individual [19]. The value of R_0 gives an idea of how quickly and extensively a disease is able to spread, where $R_0 < 1$ indicates an infection that will not permanently establish itself in a populations and $R_0 > 1$ indicates the infection will be able to invade the population [20]. Following Driessche [21], we use the next generation matrix to find R_0 . We define $\mathcal{F}_i$ to be the rate at which new

infections appear in class i and $\mathcal{V}_i$ to be the rate at which devils enter or leave class i by any other means. We find

$$F = \left[\frac{\partial \mathcal{F}_i}{\partial x_j}(x_0) \right] = \begin{bmatrix} 0 & 0 & 0 & \frac{bkS_1}{P} & \frac{bkS_1}{P} & \frac{bkS_1}{P} \\ 0 & 0 & 0 & \frac{P}{kS_2} & \frac{P}{kS_2} & \frac{P}{kS_2} \\ 0 & 0 & 0 & \frac{P}{kS_3} & \frac{P}{kS_3} & \frac{P}{kS_3} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$\text{and } V = \left[\frac{\partial \mathcal{V}_i}{\partial x_j}(x_0) \right] =$$

$$\begin{bmatrix} d_{S_1} + \frac{1}{L} & 0 & 0 & 0 & 0 & 0 \\ 0 & d_{S_2} + \frac{1}{L} & 0 & 0 & 0 & 0 \\ 0 & 0 & d_{S_3} + \frac{1}{L} & 0 & 0 & 0 \\ -\frac{1}{L} & 0 & 0 & d_I + d_{S_1} & 0 & 0 \\ 0 & -\frac{1}{L} & 0 & 0 & d_I + d_{S_2} & 0 \\ 0 & 0 & -\frac{1}{L} & 0 & 0 & d_I + d_{S_2} \end{bmatrix}$$

where x_0 is the disease free equilibrium. Then R_0 is defined as the the largest eigenvalue of FV^{-1} , which is

$$R_0 = \frac{k(d_I + d_{S_1})(S_2^* + S_3^*)(A) + b(d_I + d_{S_2})S_1^*(B)}{(d_I + d_{S_1})(d_I + d_{S_2})CAB},$$

where

$$A = (1 + d_{S_1}L),$$

$$B = (1 + d_{S_2}L), \text{ and}$$

$$C = S_1^* + S_2^* + S_3^*(1 + d_{S_1}L)(1 + d_{S_2}L).$$

Table 2: Sensitivity Index of R_0 to Parameter Values for Age-Structured Model: System (1).

Description	Parameter	Sensitivity Index
One-year-old death rate	d_{S_1}	-0.1436
Two-year-old death rate	d_{S_2}	-0.2752
Infected death rate	d_I	-0.7872
Transmission rate	k	1
Latency period	L	-0.2061
Transmission reduction	b	0.2632

For the parameters in Table 1, $R_0 = 4.025$. This high value for R_0 is consistent with the theory that DFTD started in a single female devil [22] and has become an epidemic in local devil populations. In comparison, studies on rabies in canine populations have found R_0 values of around 1.2 and 2 [23, 24]; hence, DFTD spreads more readily than rabies. Figure 6a shows that even if the one-year-old devils continue to reproduce, R_0 will not drop below one and may actually increase. Thus, the epidemic will not be curbed simply by the increased breeding rate of the one-year-old devils. In terms of r_1 ,

$$R_0 = \frac{3.99515r_1 + 0.598468}{r_1 + 0.157747}$$

and we observe that for $0 < r_1 < 1$, $3.80 < R_0 < 3.97$ as shown in Figure 6a.

The normalized forward sensitivity index of R_0 with respect to a given parameter which is given by the ratio of the relative change in R_0 , $\frac{\partial R_0}{R_0}$, to the relative change in the parameter, $\frac{\partial p}{p}$, which reduces to $\frac{\partial R_0}{\partial p} \cdot \frac{p}{R_0}$ [25].

We provide the value of the normalized forward sensitivity index of R_0 with respect to each parameter p , in Table 2. For example, the value -0.2061 for the sensitivity index of R_0 to the latency period, L means if the latency period parameter was increased from nine months to one year, an increase of 25%, we would expect R_0 to decrease by $-0.2051(.25)$ or approximately 5%. We notice that R_0 is most sensitive to the transmission rate k .

2.2 Numerical Solutions

We base our initial conditions and carrying capacity on Lachish's study in the Freycinet peninsula [26]. We assume an initial populations of 60 susceptible one-year-olds, and 35 each of susceptible two- and three-year-olds. To see how detrimental only one infected devil can be, we start with only one exposed two-year-old devil. With a 22% death rate of devils before the age of one [2], we assume an initial population of 77 under the age of one year, which would result in 60 of these devils surviving to an age of one year. We assume the initial population of 173 devils is approximately 80% the carrying capacity for

a local area. Jones [9] observed more devils breeding at younger ages once DFTD was present than prior to the introduction of DFTD due to reduced competition for resources, which resulted from the premature death of adult devils. Specifically, in the Freycinet peninsula, prior to DFTD, approximately 12.5% of one-year-old female devils mated each season, but once DFTD was established, between 40% and 60% of the one-year-old female devils mated each season [9]. For our analysis using Mathematica version 11.1 [27], we assume 40% of the one-year-olds breed. Even with an increase to 40% of one-year-old devils breeding, we see in Figure 2 the population will still decline to zero with primarily young devils making up the susceptible population, as illustrated in Figure 3. In Figure 4, we compare the disease-free graph to population trends with several one-year-old breeding rates including a value of 90%, which is the percentage of mature female devils age two years and up that breed each season. We note that if the one-year-old devil breeding rate reaches that of two- and three-year-old devils (90%), the population would stabilize but at a lower level than of that before the disease.

3 Vaccine Model

A five-year vaccination study conducted by Tovar [13] showed that it may be possible for devil populations to recover. In the study of nine healthy devils, six devils were immunized and remained disease-free, while three devils developed the disease, even though they were immunized. The devils that were vaccinated but developed DFTD, received immunotherapy where they were given a boost in cytokines to help fight off the disease [13]. We expand the age-structured model to include vaccinated classes from ages one to six. We assume β vaccinated one-year-old devils are added to the population each year with a vaccination failure rate σ for all ages up to three years old, with ratio of male to female devils added equal to that of the existing population. In the Tovar study [13], all devils who succumbed to the disease did so in less than one year, and prior to DFTD, the average lifespan of a devil was six years [1, 6]. Hence we assume vaccinated devils may potentially live up to six years, and after four years, devils will only die of non-disease related causes. Additionally, we continue to assume no vertical transmission of the vaccination, and thus, there are no vaccinated devils less than the age of one year. The age class populations, N_i , age class populations, and the total population, P , now include the appropriate vaccinated populations as well, with devils breeding up to age four [6]. The new

Figure 2: SEI populations with juvenile reproductive rate (r_1) of 40%.

Figure 3: Susceptible age classes with a juvenile reproductive rate (r_1) of 40%.

Figure 4: Population trends with varied percent of one-year-old devils breeding found in the wild [9, 26]. The disease-free population is relatively stable at approximately 150 devils, with a juvenile reproductive rate (r_1) of 12.5%, as seen pre-DFTD at the Freycinet location [9]. At the average adult reproductive rate of 90%, population is seen to become more stable with a total population for a given area maintaining a new lower level than pre-DFTD. The pre-DFTD line shows the model results without infection which maintains close to the initial population assumption.

model is given by System (2) below:

$$\begin{aligned}
 \frac{dS_0}{dt} &= yq \left(\sum_{i=1}^4 r_i N_i \right) \left(1 - \frac{P}{K} \right) - d_{s_0} S_0 - S_0 \\
 \frac{dS_1}{dt} &= S_0 - d_{S_1} S_1 - bk S_1 \frac{I}{P} - S_1 \\
 \frac{dS_2}{dt} &= S_1 - d_{S_2} S_2 - k S_2 \frac{I}{P} - S_2 \\
 \frac{dS_3}{dt} &= S_2 - d_{S_3} S_3 - k S_3 \frac{I}{P} \\
 \frac{dE_1}{dt} &= bk (S_1 + \sigma V_1) \frac{I}{P} - d_{S_1} E_1 - \frac{1}{L} E_1 \\
 \frac{dE_2}{dt} &= k (S_2 + \sigma V_2) \frac{I}{P} - d_{S_2} E_2 - \frac{1}{L} E_2 \\
 \frac{dE_3}{dt} &= k (S_3 + \sigma V_3) \frac{I}{P} - d_{S_3} E_3 - \frac{1}{L} E_3 \\
 \frac{dI_1}{dt} &= \frac{1}{L} E_1 - d_{S_1} I_1 - d_I I_1 \\
 \frac{dI_2}{dt} &= \frac{1}{L} E_2 - d_{S_2} I_2 - d_I I_2 \\
 \frac{dI_3}{dt} &= \frac{1}{L} E_3 - d_{S_3} I_3 - d_I I_3 \\
 \frac{dV_1}{dt} &= \beta - bk \sigma V_1 \frac{I}{P} - d_{S_1} V_1 - V_1 \\
 \frac{dV_2}{dt} &= V_1 - k \sigma V_2 \frac{I}{P} - d_{S_2} V_2 - V_2 \\
 \frac{dV_3}{dt} &= V_2 - k \sigma V_3 \frac{I}{P} - d_{S_3} V_2 - V_3 \\
 \frac{dV_4}{dt} &= V_3 - d_{S_4} V_4 - V_4 \\
 \frac{dV_5}{dt} &= V_4 - d_{S_5} V_5 - V_5 \\
 \frac{dV_6}{dt} &= V_5 - d_{S_6} V_6 - V_6.
 \end{aligned} \tag{2}$$

3.1 Equilibrium Values and the Basic Reproductive Number

We find an unstable disease-free equilibrium (DFE) for System (2) with parameter values from Table 1 at $S_0^* = 30.8982$, $S_1^* = 20.7371$, $S_2^* = 15.9516$, $S_3^* = 12.2705$, $V_1^* = 1.34228$, $V_2^* = 1.03252$, $V_3^* = 0.79425$, $V_4^* = 0.610961$, $V_5^* = 0.46997$, and $V_6^* = 1.56657$. The total population at this DFE is about 86 devils a reduction of approximately 50% from the initial conditions population. Susceptible baby and juvenile devils comprise 41.86% of the population, while the total vaccinated devil population comprised 6.7% of this population. The vaccine failure rate (σ) only appears in terms involving infected or exposed devils so the value of sigma will not affect the DFE values. However, the number of vaccinated devils added to the population does affect the DFE values as shown in Figure 5.

Figure 5: Susceptible, Vaccinated, and Total devil disease free equilibrium values versus number of added vaccinated devils (β).

The basic reproductive number is calculated using the next generation matrix technique defined previously and is given by

$$R_0 = \frac{k(b(G_2)(1 + d_{S_2}L)(S_1^* + \sigma V_1^*) + (G_1)(1 + d_{S_1}L)H}{(G_1)(G_2)(1 + d_{S_1}L)(1 + d_{S_2}L)D}$$

where

$$\begin{aligned} D &= S_1^* + S_2^* + S_3^* + V_1^* + V_2^*, \\ G_1 &= (d_I + d_{S_1}), \\ G_2 &= (d_I + d_{S_2}), \text{ and} \\ H &= S_2^* + S_3^* + (V_1^* + V_2^*)\sigma. \end{aligned}$$

Again, R_0 is the maximum eigenvalue of FV^{-1} , where, for the vaccine model, $F = \left[\frac{\partial \mathcal{F}_i}{\partial x_j}(x_0) \right] =$

$$\begin{bmatrix} 0 & 0 & 0 & \frac{bk(S_1+V_1)\sigma}{H} & \frac{bk(S_1+V_1)\sigma}{H} & \frac{bk(S_1+V_1)\sigma}{H} \\ 0 & 0 & 0 & \frac{k(S_2+V_2)\sigma}{H} & \frac{k(S_2+V_2)\sigma}{H} & \frac{k(S_2+V_2)\sigma}{H} \\ 0 & 0 & 0 & \frac{k(S_3+V_1)\sigma}{H} & \frac{k(S_3+V_1)\sigma}{H} & \frac{k(S_3+V_1)\sigma}{H} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

and $V = \left[\frac{\partial \mathcal{V}_i}{\partial x_j}(x_0) \right] =$

$$\begin{bmatrix} d_{S_1} + \frac{1}{L} & 0 & 0 & 0 & 0 & 0 \\ 0 & d_{S_2} + \frac{1}{L} & 0 & 0 & 0 & 0 \\ 0 & 0 & d_{S_2} + \frac{1}{L} & 0 & 0 & 0 \\ -\frac{1}{L} & 0 & 0 & d_I + d_{S_1} & 0 & 0 \\ 0 & -\frac{1}{L} & 0 & 0 & d_I + d_{S_2} & 0 \\ 0 & 0 & -\frac{1}{L} & 0 & 0 & d_I + d_{S_2} \end{bmatrix}$$

where $H = S_1 + S_2 + S_3 + V_1 + V_2 + V_3 + V_4 + V_5 + V_6$ and x_0 is the disease free equilibrium.

For the parameter values in Table 1, $R_0 = 3.92$. This is slightly lower than the R_0 of 4.025 without a vaccinated devil population but still greater than one, leading to a sustained diseased population. Hence, the DFE is unstable for System (2) [21].

Table 3: Sensitivity index of R_0 to parameter values for Vaccine Model.

Description	Parameter	Sensitivity Index
One-year-old death rate	d_{S_1}	-0.1421
Two-year-old death rate	d_{S_2}	-0.2763
Infected death rate	d_I	-0.7874
Transmission rate	k	1
Latency period	L	-0.2061
Transmission reduction	b	0.2604
Devils added	β	-0.0257
Vaccine failure	σ	0.0194

It is possible to reduce R_0 to less than one, but it would take a large influx of captive-bred, vaccinated devils, β , to be released into wild populations. In terms of β , we have

$$R_0 = \frac{4.031J - 534.73\beta + 8787}{J - 659.67\beta + 2180}$$

where

$$J = \sqrt{90.70\beta^2 + 1.592 \times 10^6\beta + 4.750 \times 10^6}.$$

In order to have the infection die out with $0 < R_0 < 1$, a minimum of 96 vaccinated devils would need to be added to the population with a maximum of 124 devils, assuming a vaccine failure rate of 25% as shown in Figure 6b. With a perfect vaccine, this minimum reduces to 56 devils with a maximum of 74. If enough devils were added to force $R_0 < 1$, then we would have a locally asymptotically stable disease-free equilibrium [21] meaning the population would be able to sustain despite introduction of the disease. While captive breeding programs continue to grow in Tasmania and throughout the world, this number of captive-bred devils being able to be released into local wild populations is an unlikely course of action.

The normalized forward sensitivity index of R_0 , $\frac{\partial R_0}{\partial p} \cdot \frac{p}{R_0}$ for each parameter is given in Table 3. We notice R_0 is not highly sensitive to either the number of devils introduced to the population β or the vaccine failure rate σ .

Using parameter values from Table 1, we have a stable endemic equilibrium of $S_0^* = 9.9534$, $S_1^* = 3.7325$, $S_2^* = 1.1468$, $S_3^* = 0.3524$, $E_1^* = 2.4087$, $E_2^* = 1.3724$, $E_3^* = 0.4217$, $I_1^* = 1.8145$, $I_2^* = 1.1581$, $I_3^* = 0.3558$, $V_1^* = 1.1210$, $V_2^* = 0.6267$, $V_3^* = 0.3504$, $V_4^* = 0.2695$, $V_5^* = 0.2073$, $V_6^* = 0.6911$ for a total of about 26 devils. This is an overall 85% population reduction where vaccinated devils comprise 11.5% of the population, while baby and juvenile devils comprise 50% of the population. In Figure 8, we see that at twenty years, the susceptible population stabilizes close to double that without the addition of vaccinated devils as seen in Figure 2. Despite the increased number of overall non-diseased devils, when we compare Figures 3 and 7 we do not see a significant

Figure 6: (a) Basic reproductive number (R_0) with one-year-old devils percent breeding using parameter values from Table 1 computed using System (1). (b) Basic reproductive number (R_0) versus the number of captive-bred, vaccinated devils released in wild populations using parameter values from Table 1 computed using System (2).

Figure 7: Total Susceptible and Vaccinated devil populations by age adding two vaccinated devils (β) with a 25% vaccination failure rate (σ).

Figure 8: SEIV devil populations adding two vaccinated devils per year (β) with a 25% vaccination failure rate (σ).

difference in the distribution of age-classes, with a continued younger population than pre-DFTD.

Figure 9a gives us the population if different number of vaccinated devils are released to the wild each year with an assumed 25% vaccine failure rate. In Figure 9b, we see the effect of adding just two vaccinated devils to the wild population each year. Note that the addition of healthy devils with no protection ($\sigma = 100\%$) almost doubles the population at twenty years, compared to no devils being added ($\beta = 0$). A perfect vaccine ($\sigma = 0\%$) gives us a sustainable devil population.

4 Conclusion

This paper illustrates the practical impacts of an increasing juvenile devil breeding frequency and of releasing captive-bred, vaccinated devils into wild, infected populations. The age-structure model shows that as the number of breeding juvenile devils increases, the local populations

may start to recover, but only if the frequency increases to a level of that of the adult breeding frequency, but this alone cannot stabilize a population in practice. The devils breed at an increased frequency as juveniles when they are able to reach the appropriate physical size needed for breeding due to a fractured age hierarchy when the disease is present, since there is reduced resource competition with the elimination of older devils. An exceptionally successful breeding season would subsequently increase resource competition, and this in turn would cause less of the next year's juveniles to reach breeding size. Regardless of the frequency at which juvenile devils breed, R_0 will continue to be between three and four, and the disease will persist. Disease control intervention is still imperative to guarantee wild population maintenance of devils in Tasmania, and continued efforts to find a viable vaccination protocol may help. Even with an imperfect vaccine, releasing vaccinated, juvenile devils into a wild, infected population can help boost local populations, but nearly 100 devils would need to be released into a local population in a given year to reduce R_0 less than one. It is

Figure 9: (a) Total devil population adding zero to five vaccinated devils per year (β) with a 25% vaccination failure rate (σ). (b) Total devil population adding two vaccinated devils per year (β) with 0–100% vaccination failure rates (σ).

much more logistically and economically viable to release two immunized devils into a local population in a given year, and our model indicates this may help to stabilize the population. We recommend breeding Tasmanian devils, vaccinating them, and strategically releasing them in locations with high potential for their survival, such as areas that have had road fencing installed to reduce vehicular death, areas where selective culling is utilized, or areas where multiple conservation techniques are used. Further modeling efforts may consider how vaccination of wild devils may help decrease disease prevalence, how natural resistance such as those devils in the West Pencil Pine location [28] may decrease disease prevalence, and how the second devil facial tumor disease (DFT2) may hurt devil populations further [29].

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