

MATHEMATICAL MODEL AND ANALYSIS OF POPULATION DYNAMICS FOR HEART FAILURE AND HEART TRANSPLANT

(Model Matematik dan Analisis Dinamik Populasi Kegagalan Jantung dan Pemindehan Jantung)

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ABSTRACT

Heart failure is a non-communicable disease that causes significant morbidity and mortality worldwide. Heart transplant is a vital treatment option for prolonging the lives of patients with heart failure. This study aims to develop a mathematical model that describes the population dynamics of heart failure and examines its stability. This model consists of three nonlinear ordinary differential equations that describe the interaction between individuals at risk of heart failure, heart failure patients, and heart transplant patients. The positivity of the solution is proven. The Routh-Hurwitz criteria are used to analyze the local stability of the equilibrium point. The global stability of the equilibrium point is established using a suitable Lyapunov function. The analysis reveals that the model has only one non-negative equilibrium point, which is found to be locally and globally asymptotically stable. Numerical simulations of the model using MATLAB are provided to verify and illustrate the analytical results. The findings of the study show that the parameters that should be controlled are the rate of acquired risk factors later in life, the probability of reversing modifiable risk factors, the progression rate from at-risk individuals to heart failure patients, the availability of heart transplant resources, the success rate of transplants, the rate of failed transplants, and the saturation factor. Control measures include implementing educational and vaccination programs, promoting lifestyle changes, conducting regular screenings, and expanding heart transplant resources. Controlling these parameters can reduce the at-risk population, decrease progression to heart failure, and improve transplant outcomes, thereby contributing to a lower overall prevalence of heart failure.

Keywords: heart failure; mathematical model; qualitative analysis; local stability; global stability

ABSTRAK

Kegagalan jantung adalah penyakit tidak berjangkit yang menyebabkan morbiditi dan kematian yang ketara di seluruh dunia. Pemindehan jantung adalah pilihan rawatan penting untuk memanjangkan hayat pesakit yang mengalami kegagalan jantung. Kajian ini bertujuan untuk membangunkan model matematik yang menerangkan dinamik populasi kegagalan jantung dan mengkaji kestabilannya. Model ini terdiri daripada tiga persamaan pembezaan biasa tak linear yang menerangkan interaksi antara individu yang berisiko mengalami kegagalan jantung, pesakit kegagalan jantung dan pesakit pemindehan jantung. Kepositifan penyelesaian model juga dibuktikan. Kriteria Routh-Hurwitz digunakan untuk menganalisis kestabilan setempat bagi titik keseimbangan. Kestabilan global bagi titik keseimbangan dibuktikan menggunakan fungsi Lyapunov yang sesuai. Analisis menunjukkan bahawa model hanya mempunyai satu titik keseimbangan bukan negatif, yang didapati stabil secara tempatan dan global secara asimptotik. Simulasi berangka model ini dijalankan menggunakan MATLAB untuk mengesahkan dan menggambarkan keputusan analitik. Dapatan kajian ini menunjukkan bahawa parameter yang perlu dikawal ialah kadar faktor risiko yang diperoleh pada akhir hayat, kebarangkalian untuk membalikkan faktor risiko yang boleh diubah, kadar perkembangan dari individu yang berisiko kepada pesakit kegagalan jantung, ketersediaan sumber pemindehan jantung, kadar kejayaan pemindehan kadar pemindehan yang gagal, dan faktor ketepuan. Langkah kawalan termasuk melaksanakan program pendidikan dan vaksinasi, mempromosikan perubahan gaya hidup,

menjalankan saringan secara berkala, dan memperluas sumber pemindahan jantung. Mengubah parameter ini boleh mengurangkan populasi yang berisiko, menurunkan kadar perkembangan kepada kegagalan jantung, dan memperbaiki hasil pemindahan, dengan itu menyumbang kepada pengurangan keseluruhan prevalens kegagalan jantung.

Kata kunci: kegagalan jantung; model matematik; analisis kualitatif; kestabilan setempat; kestabilan global

1. Introduction

Heart failure is a group of non-communicable diseases (NCDs), a primary source of morbidity and mortality worldwide, incurring a significant economic burden. The prevalence of heart failure is expected to rise (Janssen *et al.* 2008). Barnard's pioneering 1967 heart transplant led to extensive research and clinical advancements, establishing heart transplantation as a gold standard therapy for end-stage heart failure despite organ scarcity. Over the decades, expanded criteria and improved outcomes have made heart transplantation feasible for elderly patients and those with systemic diseases, marking it as a transformative achievement in modern medicine (Javier *et al.* 2021).

Although the concept of heart transplant has been contemplated for many years, early attempts faced challenges related to heart rejection. In a significant milestone in 2022, Bartley Griffith performed the world's first porcine-to-human heart transplant at the University of Maryland Medical Center in Baltimore, Maryland, marking the advent of xenotransplantation (Hawthorne 2022). Unfortunately, despite initial success, the patient's life was cut short after surviving for 2 months (Wang *et al.* 2022). The field of transplantation technology is continuously advancing, with ongoing research into alternatives to traditional organ procurement, such as using artificial organs including mechanical organs, biomechanical organs or 3D-bioprinted organs (Wang 2019).

Heart failure can either be present at birth (congenital) or acquired in later life. Risk factors that may lead to heart failure can also be classified as congenital—such as faulty valves, irregular heart rhythms, and abnormal heart muscle—or acquired in later life, including high blood pressure, diabetes, obesity, kidney disease, anemia, and other conditions (Khatibzadeh *et al.* 2013). Some risk factors may be reversible, such as smoking, alcohol consumption and obesity. Hearts for transplant can be sourced from cadaveric donors or live donors for hearts. While successful transplant surgery can extend a recipient's life, there are inherent risks associated with surgical complications. Transplant rejection, whereby the recipient's immune system attacks the transplanted organ, is common unless the transplant is between identical twins (Black *et al.* 2018). The survival rates for transplant patients at 1 year and 3 years post-transplant are approximately 52% and 48%, respectively (Hooi & Chandramalar 2018). However, even after a successful transplant, if the underlying risk factors for heart failure persist, eventual heart failure recurrence is possible, necessitating repeat heart transplantation, albeit with a lower success rate (Rana & Godfrey 2019). The scarcity of available hearts remains a significant global challenge (Alomari *et al.* 2022).

Daud and Qing (2022) developed a general linear model for non-communicable diseases and emphasised the importance of qualitative analysis instead of solely identifying the eigenvalues. Regarding the scope and methodology used in the population models, Daud highlighted various problems in the mathematical modelling of population dynamics using ordinary differential equations (Daud 2020; Daud & Qing 2022), underscoring the need for the qualitative analysis of the models (Daud 2021). While several population models of NCDs,

such as diabetes (Daud *et al.* 2020; Nasir & Mat Daud 2022), hypertension (Mat Daud *et al.* 2019), thyroid disorders (Mat Daud 2019), and anaemia (Mat Daud *et al.* 2021), have been proposed and studied in the literature, most existing models on cardiovascular disease dynamics focus primarily on clinical progression (Faes & Kerkhof 2015; Jibril & Odetunde 2020) rather than the population-level impact of heart failure. This limited focus underscores a research gap in modeling the population dynamics of heart failure to better understand progression in populations. Therefore, the objectives of this study are to construct a mathematical model for heart failure incorporating heart transplant treatment and to investigate how the subpopulations of heart failure evolve. Furthermore, this study aims to analyse the model's behaviour through stability analysis. The findings of this study may assist governmental decision-makers in formulating strategies to reduce the number of heart failure patients and prevent the progression of heart failure to critical stages. Additionally, these findings may aid in forecasting future prevalence, burden, and resource requirements (financial, material, and human resources) to manage the burden of heart failure.

The following sections are written as follows. Section 2 presents the construction of a nonlinear mathematical model for population dynamics of heart failure, focusing on qualitative analysis. Equilibrium point is identified, and stability analyses are conducted to examine the local and global behaviours of the model. Section 3 discusses the numerical simulation of the model and presents the results graphically. Section 4 comprehensively discusses the results and offers recommendations based on the findings. Finally, Section 5 provides a concise conclusion summarizing the key insights and contributions of the study.

2. Method and Results

2.1. Mathematical model

The flow diagram in Figure 1 depicts the population dynamics of heart failure as discussed in the third paragraph of Section 1. Three state variables are used to illustrate distinct phases of the condition: the number of individuals at risk of having heart failure $R(t)$, the number of heart failure patients $F(t)$, and the number of heart transplant patients $T(t)$. The saturated incidence rate, $\frac{\beta F}{(1+\gamma F)}$, reflects the ‘psychological’ effect of the inhibitory effect (Zhang & Liu 2008). $\frac{\beta}{\gamma}$ denotes the maximal supply of heart transplant resources, whereas $\frac{1}{(1+\gamma F)}$ describes the impact of heart failure patients being delayed in receiving treatment. Aside from the limitedness of heart transplant resources, the efficiency with which those resources are allocated is also essential, and it is influenced by various factors, along with the suitability of heart donors. The limitedness of the heart transplant resources, $\frac{\beta}{\gamma}$, and the efficiency of the supply of suitable heart resources, $\frac{1}{(1+\gamma F)}$, depending on the saturated treatment function (Zhou & Fan 2012). Table 1 shows thirteen constant parameters of the model.

The flow diagram in Figure 1 is then represented in a system of differential equations. The governing equations of the mathematical model are:

$$\frac{dR}{dt} = A + B - (\mu + \eta + \alpha)R + \rho T, \quad (1)$$

$$\frac{dF}{dt} = C + \alpha R - \frac{\beta F}{(1+\gamma F)} + \sigma T - (\mu + \omega)F, \quad (2)$$

$$\frac{dT}{dt} = \frac{\beta F}{(1+\gamma F)} - (\sigma + \rho + \mu + \delta)T. \quad (3)$$

with initial conditions $R(0), F(0), T(0) \geq 0$.

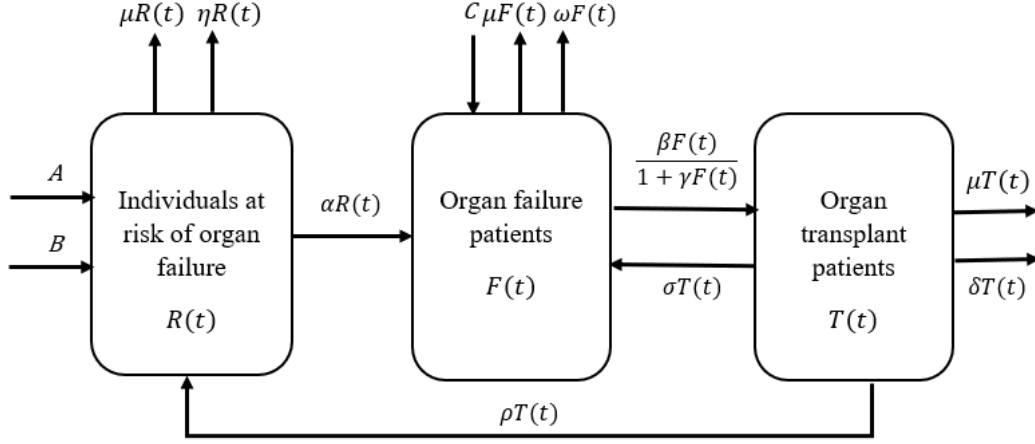


Figure 1: Flow diagram of the population dynamics of heart failure

Table 1: Parameter description

Parameter	Description
A	The rate of acquired risk factors developed at birth
B	The rate of acquired risk factors developed in later life
C	The rate of congenital heart failure
η	The probability of reversing modifiable risk factors
α	The probability of at risk individuals progressing to heart failure
β	The maximal heart transplant resources are available per unit of time.
γ	Saturation factor that assesses the effect of patients with heart failure seeking treatment.
ρ	The rate of successful transplant
σ	The rate of failed transplant
ω	The mortality rate due to heart failure
δ	The mortality rate due to heart transplant
μ	The mortality rate due to other causes

2.2. Qualitative analysis

2.2.1. Positivity of solution

In population models, positive solutions are biologically meaningful as the state variables represent the number of individuals in each subpopulation. Thus, the solutions must begin with non-negative initial conditions and maintain non-negativity throughout, reflecting the realistic nature of populations. Additionally, to ensure that the model predictions align with real-world scenarios, the population should not be able to grow indefinitely but should instead remain bounded within reasonable limits. This boundedness constraint is crucial for producing meaningful and reliable model outcomes that accurately capture the dynamics of the population under study.

Theorem 2.1. *The solution of Eq. (1)-(3) with the given non-negative initial conditions $R(0), F(0), T(0) \geq 0$ is non-negative. That is, the model solutions $R(t), F(t), T(t) \geq 0$ for all $t > 0$.*

Proof. Let $f(t) = [R(t), F(t), T(t)]$ be the solution of system under initial conditions $R(0), F(0), T(0) \geq 0$.

By the continuity of the solution, the functions $R(t), F(t), T(t)$ cannot become negative without crossing the axes $R = 0, F = 0, T = 0$.

Let $t^* = \min\{t_1, t_2, t_3\}$ where $R(t_1) = 0, F(t_2) = 0, T(t_3) = 0$ and $t_1, t_2, t_3 \geq 0$.

If $t^* = t_1$ then $R(t_1) = 0$ and the functions $F(t_1), T(t_1) > 0$ at $t = t_1$, yields

$$\frac{dR}{dt}(t^* = t_1) = A + B - (\mu + \eta + \alpha)R(t_1) + \rho T(t_1) \geq 0.$$

This ensures that at any time the function $R(t_1)$ reaches the axis $R = 0$, its $\frac{dR}{dt}$ derivative is non-negative, and the function $R(t)$ does not decrease and will not cross to negative part. We can show by similar argument that

$$\begin{aligned} \frac{dF}{dt}(t^* = t_2) &= C + \alpha R(t_2) - \frac{\beta F(t_2)}{1 + \gamma F(t_2)} + \sigma T(t_2) - (\mu + \omega)F(t_2) \geq 0, \\ \frac{dT}{dt}(t^* = t_3) &= \frac{\beta F(t_3)}{1 + \gamma F(t_3)} - (\sigma + \rho + \mu + \delta)T(t_3) \geq 0. \end{aligned}$$

This indicates that regardless of which state variable reach zero first, its derivative at that time will be non-negative and thus the state variable remains non-negative. It follows that when $t^* = 0$, $\frac{df}{dt} \geq 0$. Therefore, the solution $f(t)$ will never intersect the axes, affirming that $R(t), F(t), T(t)$ are non-negative for all $t > 0$. This concludes the proof. $\square$

2.3. Equilibrium analysis

The governing equations (1)-(3) are set to zero and solve the equations simultaneously to get the equilibrium points:

$$\begin{aligned} f_1(\hat{R}, \hat{F}, \hat{T}) &= A + B - (\mu + \eta + \alpha)\hat{R} + \rho\hat{T} = 0, \\ f_2(\hat{R}, \hat{F}, \hat{T}) &= C + \alpha\hat{R} - \frac{\beta\hat{F}}{1 + \gamma\hat{F}} + \sigma\hat{T} - (\mu + \omega)\hat{F} = 0, \\ f_3(\hat{R}, \hat{F}, \hat{T}) &= \frac{\beta\hat{F}}{1 + \gamma\hat{F}} - (\sigma + \rho + \mu + \delta)\hat{T} = 0. \end{aligned}$$

Since R, F and T represent the human populations, they must be higher than or equal to zero. The only non-negative equilibrium point of the model is given by:

$$(\hat{R}, \hat{F}, \hat{T}) = \left(\frac{A}{h} + \frac{B}{h} + \frac{\rho\beta\hat{F}}{gh(1 + \gamma\hat{F})}, \frac{-b + \sqrt{b^2 - 4ac}}{2a}, \frac{\beta\hat{F}}{g(1 + \gamma\hat{F})} \right)$$

where

$$\begin{aligned} g &= \sigma + \rho + \mu + \delta, \\ h &= \mu + \eta + \alpha, \\ k &= \mu + \omega, \\ a &= ghk\gamma, \end{aligned}$$

$$\begin{aligned} b &= (gh\beta + ghk - Cgh\gamma - \alpha Ag\gamma - \alpha Bg\gamma - \alpha\rho\beta - h\sigma\beta), \\ c &= -(Cgh + \alpha Ag + \alpha Bg). \end{aligned}$$

2.4. Stability analysis

Theorem 2.2. *The equilibrium point $(\hat{R}, \hat{F}, \hat{T})$ is locally asymptotically stable.*

Proof. From the equilibrium point $(\hat{R}, \hat{F}, \hat{T})$, the local stability matrix of the model is provided by

$$|J_1 - \lambda I| = \begin{vmatrix} -(\mu + \eta + \alpha) - \lambda & 0 & \rho \\ \alpha & -\frac{\beta}{(1+\gamma\hat{F})^2} - (\mu + \omega) - \lambda & \sigma \\ 0 & \frac{\beta}{(1+\gamma\hat{F})^2} & -(\sigma + \rho + \mu + \delta) - \lambda \end{vmatrix}.$$

where λ are eigenvalues, I is the matrix identity, and J_1 is the Jacobian matrix of the model.

The characteristic equation of the model (1) around $(\hat{R}, \hat{F}, \hat{T})$ is given by

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0, \quad (4)$$

where

$$\begin{aligned} a_1 &= 3\mu + \sigma + \rho + \delta + \omega + \eta + \alpha + \frac{\beta}{(1+\gamma\hat{F})^2}, \\ a_2 &= \frac{\beta(\rho+\mu+\delta)}{(1+\gamma\hat{F})^2} + (\mu + \omega)(\sigma + \rho + \mu + \delta) + (\mu + \eta + \alpha) \\ &\quad \left(2\mu + \sigma + \rho + \delta + \omega + \frac{\beta}{(1+\gamma\hat{F})^2}\right), \\ a_3 &= \frac{(\mu+\eta)\beta\rho+\beta(\mu+\delta)(\mu+\eta+\alpha)}{(1+\gamma\hat{F})^2} + (\mu + \omega)(\sigma + \rho + \mu + \delta)(\mu + \eta + \alpha). \end{aligned}$$

When the determinants of all Hurwitz matrices are positive,

$$\det(H_1) > 0, \det(H_2) > 0, \det(H_3) > 0.$$

By the Routh-Hurwitz criteria of polynomial order 3, all roots of Eq. (4) are negative or have negative real parts if $a_1 > 0$, $a_3 > 0$, and $a_1a_2 - a_3 > 0$.

It is obvious that $a_1 > 0$ and $a_3 > 0$. We calculate $a_1a_2 - a_3$ as follows:

$$a_1a_2 - a_3 = \left(2\mu + \sigma + \rho + \delta + \omega + \alpha + \frac{\beta}{(1+\gamma\hat{F})^2}\right) \frac{\beta\rho}{(1+\gamma\hat{F})^2}$$

$$\begin{aligned}
 & + \left(3\mu + \sigma + \rho + \delta + \omega + \eta + \alpha + \frac{\beta}{(1+\gamma\hat{F})^2} \right) \frac{\beta(\mu+\delta)}{(1+\gamma\hat{F})^2} \\
 & + \left(2\mu + \sigma + \rho + \delta + \omega + \frac{\beta}{(1+\gamma\hat{F})^2} \right) (\mu + \omega)(\sigma + \rho + \mu + \delta) \\
 & + \left(2\mu + \sigma + \rho + \omega + \eta + \alpha + \frac{\beta}{(1+\gamma\hat{F})^2} \right) (\mu + \eta + \alpha) \\
 & \quad \left(2\mu + \sigma + \rho + \delta + \omega + \frac{\beta}{(1+\gamma\hat{F})^2} \right) \\
 & + (\mu + \delta)(\mu + \eta + \alpha)(2\mu + \sigma + \rho + \delta + \omega) > 0.
 \end{aligned}$$

Therefore, $(\hat{R}, \hat{F}, \hat{T})$ is locally asymptotically stable without restrictions on the parameter values. $\square$

Theorem 2.3. *The equilibrium point is globally asymptotically stable.*

Proof. It is assumed that the population size $N = R + F + T$ is constant. Then, substituting $R = N - F - T$ in equation 1(b), the model can be rewritten as

$$\begin{aligned}
 \frac{dF}{dt} &= C + \alpha R - f(F, T) - (\mu + \omega + \alpha)F, \\
 \frac{dT}{dt} &= f(F, T) - (\alpha + \rho + \mu + \delta)T.
 \end{aligned}$$

where

$$f(F, T) = \frac{\beta F}{(1+\gamma F)} + (\alpha - \sigma)T.$$

Note that, in reality (Hsich 2016), $\alpha > \sigma$. (This is due to the limited resources available for heart transplantation and the relatively small number of patients who have undergone heart transplantation compared with those at risk of developing heart failure).

The equation (1) for the risk of the heart failure population, which in this case, is

$$\frac{dR}{dt} = A + B - (\mu + \eta)R - \alpha R + \rho T,$$

can be omitted as the constant population size assumption enables us to do that.

Since all parameters are positive and $F, T > 0$, $f(F, T)$ is a positive function. $f(F, T)$ is monotonically growing function for all $F, T > 0$, because

$$\frac{\partial f}{\partial F} = \frac{\beta}{(1+\gamma F)^2} > 0, \frac{\partial f}{\partial T} = \alpha - \sigma > 0.$$

At equilibrium,

$$\begin{aligned}
 C + \alpha R &= f(F^*, T^*) + (\mu + \omega + \alpha)F^*, \\
 f(F^*, T^*) &= (\alpha + \rho + \mu + \delta)T^*.
 \end{aligned}$$

Consider a Lyapunov function (Korobeinikov 2006)

$$V(F, T) = \int_{F^*}^F \left(1 - \frac{f(F^*, T^*)}{f(\tau, T^*)}\right) d\tau + \int_{T^*}^T \left(1 - \frac{f(F^*, T^*)}{f(F^*, \tau)}\right) d\tau.$$

It is obvious that $V \geq 0$ and $V = 0$ if and only if $F = F^*, T = T^*$.

$$\begin{aligned} \frac{\partial V}{\partial F} &= 1 - \frac{f(F^*, T^*)}{f(F, T^*)}, \quad \frac{\partial V}{\partial T} = 1 - \frac{f(F^*, T^*)}{f(F^*, T)} \\ \frac{\partial^2 V}{\partial F^2} &= \frac{f(F^*, T^*)}{(f(F, T^*))^2} \frac{\partial f(F, T^*)}{\partial F}, \quad \frac{\partial^2 V}{\partial T^2} = \frac{f(F^*, T^*)}{(f(F^*, T))^2} \frac{\partial f(F^*, T)}{\partial T}. \end{aligned}$$

Next, our task is to show that $\frac{dV}{dt} \leq 0$ for all $F, T > 0$.

$$\begin{aligned} \frac{dV(F, T)}{dt} &= \frac{dF}{dt} - \frac{f(F^*, T^*)}{f(F, T^*)} \frac{dF}{dt} + \frac{dT}{dt} - \frac{f(F^*, T^*)}{f(F^*, T)} \frac{dT}{dt} \\ &= C + \alpha R - f(F, T) - (\mu + \omega + \alpha)F \\ &\quad - \left(\frac{f(F^*, T^*)}{f(F, T^*)}\right) (C + \alpha R - f(F, T) - (\mu + \omega + \alpha)F) \\ &\quad + f(F, T) - (\alpha + \rho + \mu + \delta)T \\ &\quad - \left(\frac{f(F^*, T^*)}{f(F^*, T)}\right) (f(F, T) - (\alpha + \rho + \mu + \delta)T). \end{aligned}$$

Using function

$$\begin{aligned} C + \alpha R &= f(F^*, T^*) + (\mu + \omega + \alpha)F^*, \\ f(F^*, T^*) &= (\alpha + \rho + \mu + \delta)T^*, \end{aligned}$$

we get

$$\begin{aligned} \frac{dV(F, T)}{dt} &= (\mu + \omega + \alpha)F^* \left(1 - \frac{F}{F^*}\right) \left(1 - \frac{f(F^*, T^*)}{f(F, T^*)}\right) \\ &\quad + f(F^*, T^*) \left(1 - \frac{f(F^*, T^*)}{f(F, T^*)}\right) \left(1 - \frac{f(F, T)}{f(F^*, T)}\right) \\ &\quad + f(F^*, T^*) \left(\frac{T}{T^*} - \frac{f(F, T)}{f(F, T^*)}\right) \left(\frac{f(F^*, T^*)}{f(F^*, T)} - 1\right). \end{aligned}$$

The monotonicity of $f(F, T)$ with respect to F ensures that function

$$\left(1 - \frac{F}{F^*}\right) \left(1 - \frac{f(F^*, T^*)}{f(F, T^*)}\right) \leq 0$$

and

$$\left(1 - \frac{f(F^*, T^*)}{f(F, T^*)}\right) \left(1 - \frac{f(F, T)}{f(F^*, T)}\right) \leq 0$$

hold for all $F, T > 0$. Moreover,

$$\left(\frac{T}{T^*} - \frac{f(F, T)}{f(F, T^*)}\right) \left(\frac{f(F^*, T^*)}{f(F^*, T)} - 1\right) \leq 0$$

if $\frac{f(F,T)}{f(F,T^*)} \geq \frac{T}{T^*}$ when $f(F^*, T^*) \geq f(F^*, T)$, and $\frac{f(F,T)}{f(F,T^*)} \leq \frac{T}{T^*}$ when $f(F^*, T^*) \leq f(F^*, T)$ holds for all $F, T > 0$. If equilibrium is positive and the function $f(F, T)$ is concave with respect to T (that is, if $\frac{\partial^2 f(F,T)}{\partial T^2} \leq 0$ holds), then $\frac{dV}{dt} \leq 0$ for all $F, T > 0$.

For a monotonic function, $f(F^*, T) \geq f(F^*, T^*)$ implies $T \geq T^*$, and $f(F^*, T) \leq f(F^*, T^*)$ implies $T \leq T^*$, hence the condition is equivalent to the condition $\frac{f(F,T)}{f(F,T^*)} \geq \frac{T}{T^*}$ for all $T \leq T^*$ and $\frac{f(F,T)}{f(F,T^*)} \leq \frac{T}{T^*}$ for all $T \geq T^*$. This condition holds for all functions concave with respect to the variable T ; hence the concavity is sufficient to ensure that $\frac{dV(F,T)}{dt} \leq 0$.

It is obvious that for a monotonic function, the equilibrium point is the only invariant point of the system in the set $\frac{dV}{dt} = 0$. Therefore, the equilibrium is asymptotically stable in the non-negative quadrant by the Lyapunov-La Salle principle (Khalil 2002). $\square$

3. Numerical Simulation

To illustrate the theoretical results, consider the following set of parameters and initial conditions:

$$\begin{aligned} A &= 3,000, B = 1,000,000, C = 2,000, \eta = 0.04, \alpha = 0.009, \beta = 0.85, \\ \gamma &= 0.2, \rho = 0.1, \sigma = 0.1, \omega = 0.004084, \mu = 0.004721, \delta = 0.1, \\ R_0 &= 21,840,000, F_0 = 2,090,400, T_0 = 3. \end{aligned}$$

and the corresponding equilibrium point is $(\hat{R}, \hat{F}, \hat{T}) = (18,670,564, 19,310,872, 13)$. The estimated parameters' values are used to perform numerical simulation to verify and illustrate our theoretical results. Table 2 shows the estimated parameter values and their sources.

Table 2: Estimated parameter values

Parameter	Value	Source
A	3,000 year ⁻¹	Ministry of Health Malaysia (2007)
B	1,000,000 year ⁻¹	Assumed
C	2,000 year ⁻¹	Ministry of Health Malaysia (2007)
η	0.04 year ⁻¹	Institute for Public Health (2015; 2019)
α	0.009 year ⁻¹	Savarese & Lund (2017)
β	0.85 year ⁻¹	Assumed
γ	0.2 year ⁻¹	Frierson et al. (1990); Long et al. (2002)
ρ	0.1 year ⁻¹	Chandramalar & Sulaiman (2016)
σ	0.1 year ⁻¹	Chandramalar & Sulaiman (2016)
ω	0.004084 year ⁻¹	Department of Statistics Malaysia (2016); Ministry of Health Malaysia (n.d.)
δ	0.1 year ⁻¹	Chandramalar & Sulaiman (2016)
μ	0.004721 year ⁻¹	Department of Statistics Malaysia (2016)
τ	14.1 years	Tackling & Borhade (2023)
R	21,840,000 individuals year ⁻¹	Ministry of Health Malaysia (2016)
F	2,090,400 individuals year ⁻¹	Savarese & Lund (2017)
T	3 individuals year ⁻¹	Chandramalar & Sulaiman (2016)

The behaviour of the state variables in the proposed model are using the estimated population data related to heart failure. The number of individuals at risk of heart failure, $R(t)$, is depicted in Figure 2. Figure 3 shows the number of heart failure patients, $F(t)$, while Figure 4 shows the number of heart transplant, $T(t)$. The number of individuals at risk of heart failure patients, $R(t)$ is higher than the number of heart failure patients, $F(t)$ while the number of heart transplant patients, $T(t)$ is the lowest and remains constant over time, as seen in the graph.

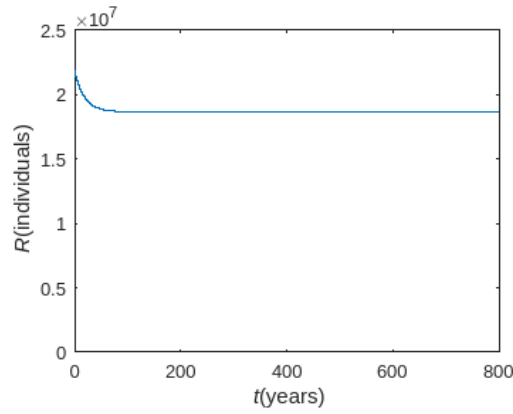


Figure 2: Number of individuals at risk of heart failure patients against time, $R(t)$

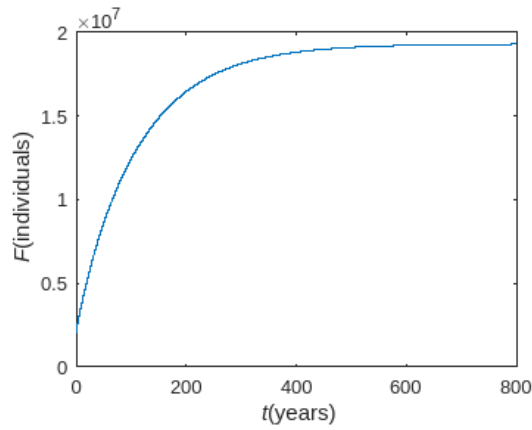


Figure 3: Number of heart failure patients against time, $F(t)$

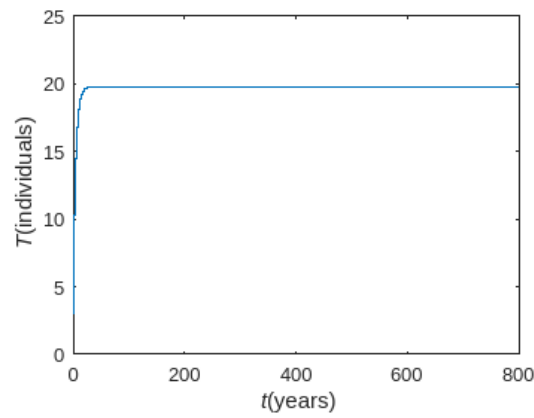


Figure 4: Number of heart transplant patients against time, $T(t)$

Figure 5-11 displays the solution trajectories of the system by varying some specific parameters, including acquired risk factors in later life, B , the probability of reversing modifiable risk factors, η , and the probability of at-risk individuals progressing to heart failure, α , the availability of heart transplant resources, β , the rate of successful transplants, ρ , the rate of failed transplants, σ , and the saturation factor, γ .

In Figure 5, the analysis addresses the effect of reducing the number of individuals who acquire risk factors in later life, B , which results in a decline in both the number of individuals at risk of heart failure, $R(t)$, and the number of heart failure patients, $F(t)$. The number of heart transplant patients, $T(t)$ remains relatively unaffected as T depends on factors specific to heart failure progression and transplant availability rather than initial risk acquisition. More precisely, decreasing parameter B from 1,000,000 to 100,000 resulted in a significantly lower number of individuals in both R and F compared to when B is 500,000. This figure illustrates that the fewer individuals who acquire risk factor in later life, the lower the number of those at risk of heart failure, ultimately reducing the number of heart failure patients. Conversely, an increase in the rate of this parameter escalates the disease's dynamics.

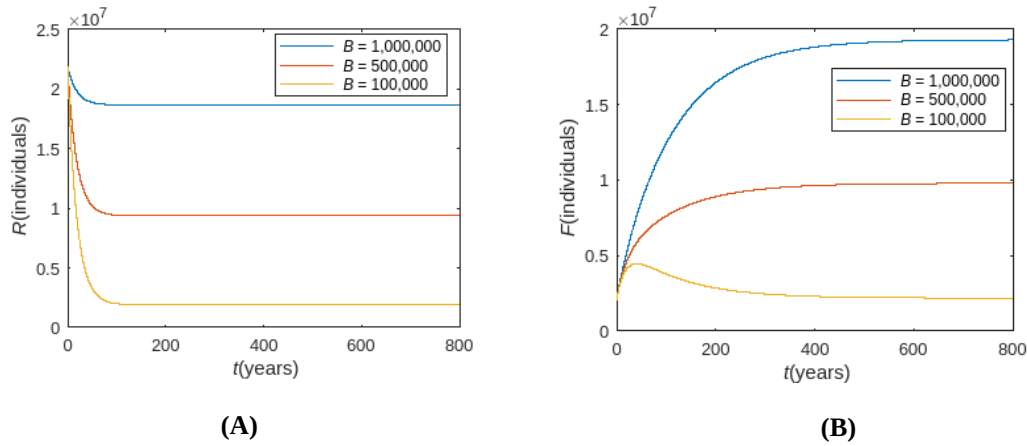


Figure 5: (A) Effect of varying B values (1,000,000, 500,000, and 100,000) on R ; (B) Effect of varying B values (1,000,000, 500,000, and 100,000) on F

The numerical simulation of the system by varying the rate of at-risk individuals progressing to heart failure, α , reveals that decreasing α from 0.009 to 0.001 results in a significant increase in R compared to when $\alpha = 0.005$. This is because a lower α indicates a slower rate of progression from R to F , thereby increasing the population size of R . T remains unchanged because α does not directly influence the transition rates related to transplants. Conversely, the decreased values of α leads to a decrease in F . On the other hand, reducing the values of the rate of failed transplants, σ , from 0.10 to 0.01 leads to an increase in the T , with no significant change in R and F . A lower σ allows more patients to remain in the T and have a direct impact on T , rather than being lost to transplant failure. The impacts of changes in both parameters are illustrated in Figures 6 and 7.

Conversely, an increase in the probability of reversing modifiable risk factors, represented by η , from 0.04 to 0.10 and 0.50, leads to a significant decrease in both R and F also. This adjustment notably reduces the overall population afflicted with heart failure without affecting

T , since η impacts only the reduction of risk factors rather than any transition associated with transplants. The changes is shown in the Figure 8.

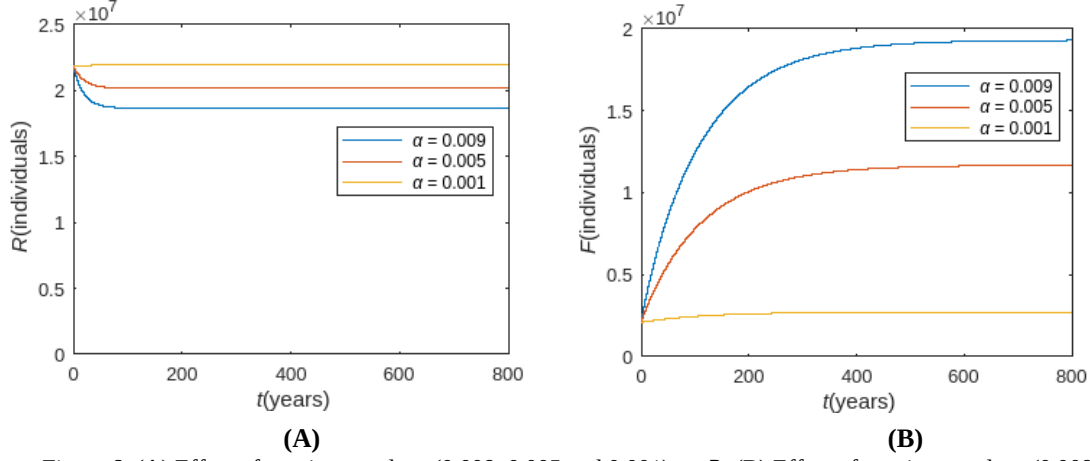


Figure 6: (A) Effect of varying α values (0.009, 0.005 and 0.001) on R ; (B) Effect of varying α values (0.009, 0.005 and 0.001) on F

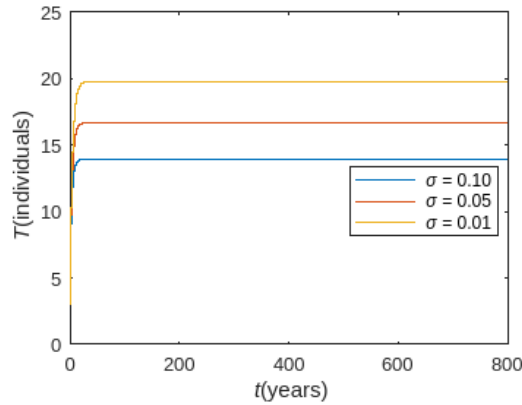


Figure 7: Effect of varying σ values (0.10, 0.05 and 0.01) on T

Enhancing the availability of heart transplant resources, β , from 0.85 to 1.00 and 2.00, facilitates the recovery of T through appropriate heart transplants as shown in Figure 9. Furthermore, elevating the rate of successful transplants, ρ , from 0.10 to 0.50 and 0.80 in Figure 10, leads to a decrease in T and recovery from heart failure.

Additionally, increasing the saturation factor, γ , from 0.2 to 0.5 and 1.0 effectively reduces the number of T and recovery from heart failure in Figure 11. This is because the higher saturation levels indicate greater limitations in transplant availability, resulting in fewer individuals receiving transplants due to the constraints on the transplant system's capacity. These adjustments do not affect R and F because they only impact the transplant-related transitions. However, as illustrated in Figure 5 to 11, modifications in these parameters do not significantly influence the number of heart transplant patients over time.

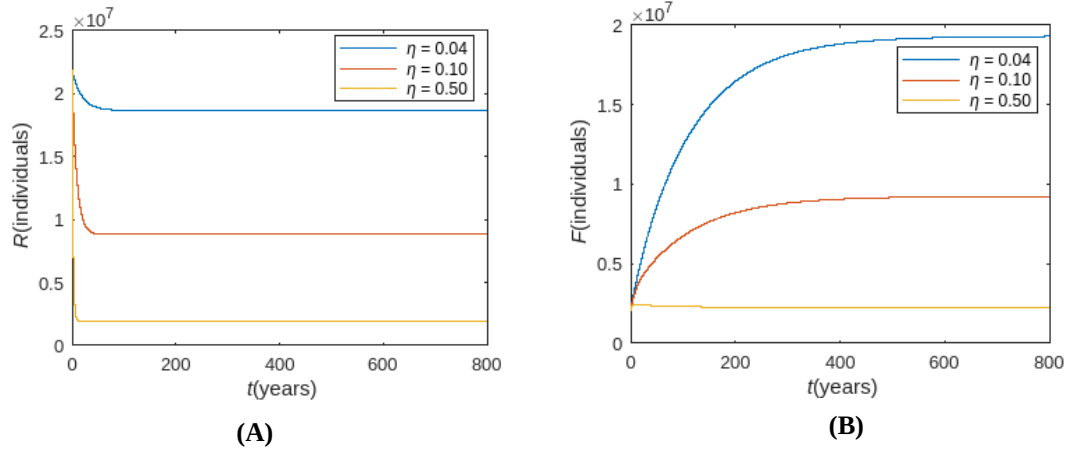


Figure 8: (A) Effect of varying η values (0.04, 0.10 and 0.50) on R ; (B) Effect of varying η values (0.04, 0.10 and 0.50) on F

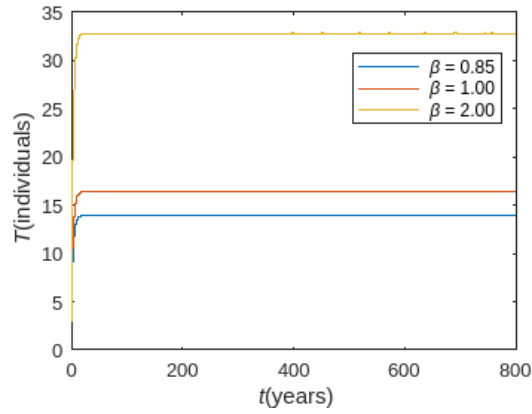


Figure 9: Effect of varying β values (0.85, 1.00 and 2.00) on T

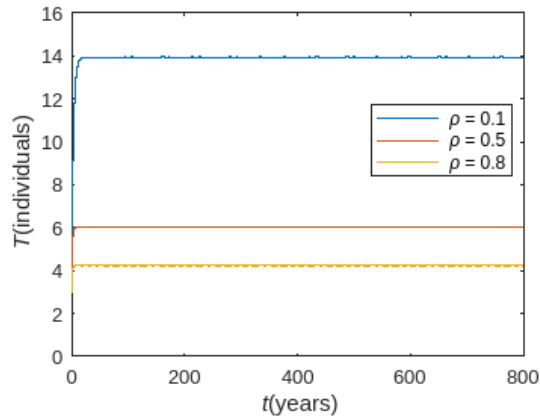


Figure 10: Effect of varying ρ values (0.1, 0.5 and 0.8) on T

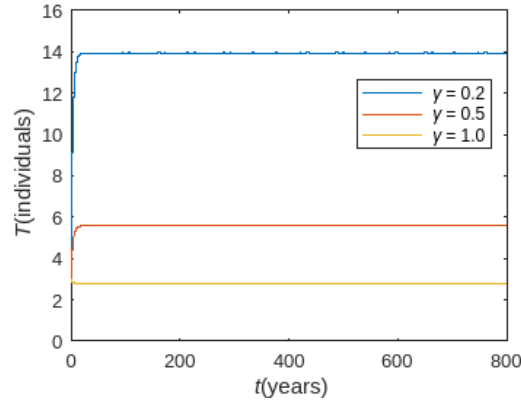


Figure 11: Effect of varying γ values (0.2, 0.5 and 1.0) on T

4. Discussion

The mathematical model presented offers valuable insights into the dynamics governing the prevalence and progression of heart failure within a population. The population will approach one equilibrium point, which is locally and globally asymptotically stable. The equilibrium analysis facilitates understanding of the relationship between parameters at equilibrium point. In the context of reducing the population of heart failure, it is essential to consider modifications to parameters to achieve a more favorable equilibrium point.

Reducing the rates of acquired risk factors set in later life, B , increasing the probability of reversing modifiable risk factors, η , and lowering the probability of at-risk individuals progressing to heart failure, α , are vital in reducing the heart failure population. Addressing these three parameters involves primary prevention, secondary prevention, and rehabilitation. Primary prevention involves various strategies. Firstly, educational programs may cultivate healthy lifestyles through health promotion campaigns and healthy living syllabi in school curricula. Secondly, health initiatives through vaccination may prevent infections that increase the risks of heart failure, such as Hepatitis B, Tuberculosis and Pneumococcal vaccination (Bhatt *et al.* 2017). Thirdly, developing a conducive environment may promote healthy lifestyles by providing suitable infrastructure (such as exercise facilities) and implementing town planning that encourages walking or cycling. Fourthly, enacting legislation may reduce substance use by controlling harmful substances. Fifthly, financial initiatives may be introduced to improve healthy living (such as subsidies or tax relief for healthy diet or exercise programs) and discourage unhealthy living (such as taxes for processed food). These are merely examples of primary preventions and the list is not exhaustive. Besides primary prevention, secondary prevention is also imperative through regular screenings for early detection of potential diseases which may increase the risk factors for heart failures (such as dyslipidemia, diabetes, and hypertension) to allow appropriate management of these diseases to slow down the progression to heart failure (Ministry of Health Malaysia 2017). Reversing the modifiable risk factors, η , also require rehabilitation programs to facilitate lifestyle changes through psychological and pharmaceutical interventions, as well as support systems.

To reduce the population of heart failure, it is also essential to increase the availability of heart transplant resources, β , increase the rate of successful transplants, ρ , minimise the rate of failed transplants, σ , and increase the saturation factor, γ . These involve increasing heart procurement, training specialist human resources, providing adequate facilities, and improving

transplantation technology from the technical and ethical aspects. Heart donation campaigns may increase awareness and participation of the lay public in their potential role in extending the lives of heart-failure patients. Promoting research and development in artificial hearts and addressing its ethical considerations is imperative, as it has the potential to provide an unlimited supply of hearts for transplantation in the future without introducing new ethical issues. Various strategies ought to be implemented to improve the availability of human resources (such as scholarships and incentives for specialists) and facilities (such as incentives for investors in the healthcare sector). Improving transplantation technology and techniques requires the combined effort of many researchers in the fields of medicine, allied health, pharmacology, and biomedical engineering.

Implementing all the strategies to reduce the heart failure population requires immense resources. However, since the present mathematical model does not include sensitivity analysis, future studies should aim to conduct sensitivity analysis to identify the parameters with the greatest effects on reducing heart failure patients.

5. Conclusion

This study proposes a model to describe the population dynamics of heart failure population. The positivity of the solution is studied. The model has a unique non-negative equilibrium point. The equilibrium point is found to be locally and globally asymptotically stable. By examining how the equilibrium point is influenced by the model parameters, we can determine which parameters increase or decrease the population size. Incorporating the heart transplant variable into the mathematical model provides valuable insights into how heart transplants, coupled with the limited supply of donor hearts, impact the dynamics of the heart failure population. Additionally, it allows the model to examine how an unlimited supply of organs—such as xenografts, mechanical hearts, biomechanical hearts, or 3D-bioprinted hearts—would alter these dynamics. Hence, the modellers can create an iterative tool to simulate different scenarios and visualise different possible outcomes under various interventions. However, the absence of sensitivity analysis made it difficult to determine which parameter most significantly affects the heart failure population. This highlights potential research gaps that could be addressed in future studies.

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