# Effects of Lifestyle Choices on Atherosclerosis
## A Mathematical Approach

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### Abstract

Cardiovascular diseases (CVDs) cause more than 40% of all deaths in America [5, 6]. Genetic predisposition and lifestyles choices such as smoking, poor nutrition, physical inactivity and other negative behavioral actions are common risk factors that increase the probability of developing CVDs. We construct a mathematical model of nonlinear differential equations to describe the dynamics of *atherosclerosis*, a precursor to other cardiovascular diseases. We divide the population by low and high genetic predisposition to developing CVDs. The population is then divided into healthy and unhealthy classes based on modifiable and non-modifiable lifestyles. We focus on two populations: African Americans and Caucasian Americans because of their different genetic predispositions to CVDs. The basic reproductive number, $R_0$, is calculated. Local stability of the unhealthy-free equilibrium is established. A sensitivity and uncertainty analysis is performed on the basic reproductive number. We conclude that the number of interactions between healthy and unhealthy individuals play a key role in reducing the progression to atherosclerosis.

## 1 Introduction

Atherosclerosis (formation of plaque along the inner lining of medium to large arteries) is a type of Cardiovascular Disease (CVD) that can develop throughout the entire circulatory system. It is a condition that leads to the development of various CVDs, including some highly fatal conditions such as stroke and coronary heart disease (CHD) [3]. The plaque consists of fatty deposits, cholesterol and other atherogenic substances that build up and harden along the artery wall dramatically narrowing arterial passageways [4,

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8]. Atherosclerosis reduces blood flow and creates wall shear stress, the magnitude of the frictional force applied to the inner linings of the artery wall by the flow of blood within arteries [4, 8]. Blood flow through the carotid and coronary arteries is essential to ensure that oxygen reaches the brain and heart. If an individual develops arterial stenosis (a case of atherosclerosis in the carotid or coronary arteries) there is a high probability that stroke, myocardial infarction (MI) or death may occur. Such traumas result from atherosclerotic disease.

Most CVDs are prevalent in individuals between the ages of 40 and 79 and are the leading cause of death in the United States, accounting for approximately one million deaths in the United States each year [5, 6].

Risk factors of atherosclerosis are divided into two categories: non-modifiable and modifiable. The non-modifiable genetic risk factors include age, gender, race and genetically inherited diseases such as diabetes (type I). The modifiable risk factors have the potential to change, i.e., the excessive use of alcohol, poor exercise habits, poor nutrition, and smoking among others [17]. These factors increase an individual's probability of developing atherosclerosis. Poor eating habits are modifiable risk habits that can lead to Diabetes mellitus (type II), a disease known to increase one's probability of developing atherosclerosis. Other risk factors are attributed to genetic predisposition, as well as lifestyle choices. Hypertension (high blood pressure) and dyslipidemia (high cholesterol) are examples of hereditary diseases that an individual can develop over time if they adopt an unhealthy lifestyle.

Arterial blockage due to atherosclerosis can be diagnosed via duplex ultrasound and magnetic resonance angiography (MRA) [19]. Once significant narrowing of the arteries due to atherosclerosis is diagnosed, proper treatment can be administered. Individuals with over 60% diameter reduction of main arteries are advised to have an endarectomy (a surgical procedure to eliminate plaque), while angioplasty is performed in cases where the diameter is reduced by 50% or less [5].

We explore risk factors that minimize the progression to atherosclerosis. We determine the most sensitive lifestyle parameters related to modifiable and non-modifiable risk factors, and we model "unhealthiness" as a contagious disease that spreads as a result of interactions between individuals with a healthy lifestyle and individuals with an unhealthy lifestyle. Such contacts include peer pressure among other social interactions. The paper is organized as follows: Section 2 provides an overview of cardiovascular diseases. Section 3 introduces a mathematical model of behavioral interactions based on lifestyle choices, and discusses parameter values, as well as, the reproductive number, $R_0$. In Section 4 we summarize our results; we provide a discussion of our results and present ideas for furthering studies in the last section. Detailed computations can be found in the appendices.

## 2 Cardiovascular Diseases: An Overview

Cardiovascular diseases involve both the heart and blood vessels. While arteries transport oxygen-rich blood to the rest of body the veins carry oxygen depleted blood [1]. Of the 70.1 million Americans with CVDs, 27 million are age 65 or older [21]. The Framingham Heart Study determined the risk factors for the development of CVDs 30 years ago [21]. This study established age, gender, diabetes, hypertension, dyslipidemia (high cholesterol), and smoking as the important risk factors of CVDs. Today, the American Heart Association continues to acknowledge these same risk factors for Cardiovascular Diseases along with additional factors including physical inactivity and other negative behavioral actions [21]. There are two classes of CVDs: heart diseases and blood vessel related diseases. Cardiovascular heart diseases include congestive heart failure, coronary heart disease, angina, congenital cardiovascular defects and arrhythmia. Blood vessel related CVDs include coronary artery disease, hypertension, atherosclerosis and stroke.

Atherosclerosis is a precursor to many cardiovascular diseases including: stroke, coronary heart disease, aortic aneurysms and arrhythmias [21]. Arterial stenosis, the hardening of the arteries, is a late stage of atherosclerosis. Risk factors for the development of atherosclerosis include smoking, high blood pressure, high cholesterol, type (II) diabetes, obesity, physical inactivity, heredity, socioeconomic factors, and other behavioral factors [12]. Conditional risk factors of atherosclerosis include homocysteine, and fibrinogen. Homocysteine is an amino acid that forms during the metabolic process [12]. High amounts of homocysteine levels in the plasma may accelerate the progression to developing atherosclerosis [12]. Fibrinogen is an important type of protein that affects plasma viscosity during coagulation, the process that allows blood to clot. Methods used to treat atherosclerosis include surgery, angioplasty (stenting), and prescription blood thinners.

A stroke occurs when brain cells are deprived of oxygen-rich blood [15]. According to the American Heart Association about 700,000 individuals in the United States suffer a stroke each year [8]. African-Americans, American Indians or Alaskan Natives and Mexican Americans are at a higher risk of suffering a stroke than Caucasian Americans. Of the individuals who suffer stroke, 500,000 are first attacks, while the remaining 200,000 are recurrent attacks [21]. There are two types of strokes ischemic and hemorrhage. An ischemic stroke occurs when a blood clot forms in the neck or brain. Blood clots, however, can originate in other areas of the body and cause a stroke. Ischemic strokes occur over 80% of the time [15]. Risk factors for this type of stroke are hypertension, smoking, diabetes, asymptomatic carotid stenosis (atherosclerosis), atrial fibrillation, high cholesterol (lipids), physical inactivity, poor diet, alcohol and drug abuse. By checking blood pressure regularly, monitoring blood sugar levels, taking prescribed medica-

tions regularly, and by controlling behavior changes such as good diet and exercise an individual can prevent ischemic stroke [11].

Hemorrhage strokes have a higher death rate and occur when blood vessels break and blood leaks to the brain [13]. Risk factors include high blood pressure, heart disease, smoking, diabetes, hereditary, age, gender, race, obesity, excessive alcohol consumption, stress, high cholesterol, high fat consumption and high sodium intake [13]. According to the National Center of Health Statistics (NCHS) and National Heart Lung and Blood Institute (NHLBI), males have a 1.25% greater incidence rate than females. While the overall stroke incidence is 2.6% for the total population (5, 400, 000 in 2002). In 2002 about 1 in every 15 deaths in the United States was due to stroke [21].

Ultrasounds, Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) scans are the standard methods used to detect and diagnose CVDs. Currently, researchers in mathematics, engineering and medicine are conducting research in cardiovascular imaging, imaging blood vessels with magnetic fields to improve imaging analysis [14]. Dr. Ed DiBella of the Utah Center for Advanced Imaging Research (UCAIR) is currently performing a study in dynamic imaging with MRI and Positron Emission Tomography (PET)[16]. He developed an automated analysis method to model quantitative kinetics to find precise parameter values. Before 1990, the only way to diagnose intracranial vascular disease was by inserting a catheter into the arteries that supply blood to the head, injecting a contrast agent (dye) into the blood stream and then taking X-ray images of the head.

## 3  Formulation of the Model

The population is divided into *low* (*L*) or *high* (*H*) genetic predisposition classes through non-modifiable risk factors. We assumed that individuals with low genetic low genetic predisposition enter the model through the corresponding healthy class, whereas individuals with high genetic predisposition can enter the system directly through their corresponding healthy or infected class, $S_{Hh}$ and $I_H$, respectively. One's genetic predisposition to atherosclerosis cannot change. Therefore, we model the effects of lifestyle changes on the number of diagnosed cases of atherosclerosis. Modifiable lifestyle choices can increase or decrease the probability of progression to atherosclerosis [3]. As a result, individuals from either low or high genetic risk classes can change their susceptibility to the disease based on social interactions with unhealthy individuals. A detailed explanation of the parameters and values are discussed in Section 4.

Individuals with low genetic predisposition to atherosclerosis may live a healthy or unhealthy lifestyle, $S_{L_h}$ or $S_{L_u}$, respectively. Total birth rate is $\Lambda$, of which $p\Lambda$ enters into genetically low and the remaining of the new births $(1-p)\Lambda$ go to genetically high. As defined by the World Health Organization (WHO), a healthy person has proper nutrition, exercises regularly,

does not smoke or abuse alcohol and manages stress well. An unhealthy person is defined to have poor nutrition, poor exercise habits, smokes regularly, abuses alcohol and doe not manage stress well [22]. Healthy individuals with low genetic predisposition to atherosclerosis ($S_{L_h}$) may adopt an unhealthy lifestyle and move to the unhealthy class ($S_{L_u}$) when they come in contact with unhealthy individuals ($S_{L_u}$ and $S_{H_u}$). Once in $S_{L_u}$, individuals develop the disease and progress to the infected class ($I_L$). We assume that individuals who change their lifestyle from healthy to unhealthy can only go back to living a healthy life after they encounter cardiovascular complications.

Individuals with high genetic predisposition to atherosclerosis are divided into two groups. A fraction, $(1 - p)r\Lambda$, of new births naturally develops atherosclerosis and enters the system by vertical transmission into the infected class. A fraction, $(1 - p)(1 - r)\Lambda$, of new births enters the model through the genetically high healthy class. Individuals can live either healthy or unhealthy lifestyles ($S_{H_h}$ or $S_{H_u}$). Individuals enter the system as healthy individuals with high genetic predisposition ($S_{H_h}$) and can develop an unhealthy lifestyle and move to the unhealthy class ($S_{H_u}$) when they come in contact with unhealthy individuals ($S_{L_u}$ and $S_{H_u}$).
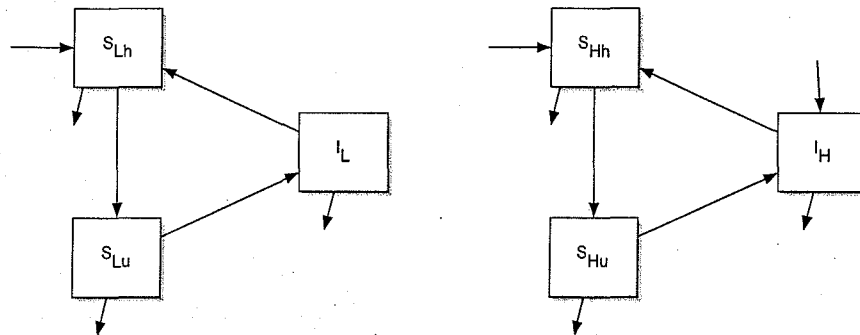


Figure 1: Caricature of the model

$$S'_{L_h} = p\Lambda - \rho_1 S_{L_h}\frac{S_{L_u} + S_{H_u}}{N} + \gamma_1 I_L - \mu S_{L_h} \tag{1}$$

$$S'_{L_u} = \rho_1 S_{L_h}\frac{S_{L_u} + S_{H_u}}{N} - (\alpha_1 + \mu)S_{L_u} \tag{2}$$

$$I'_L = \alpha_1 S_{L_u} - (\nu_1 + \gamma_1 + \mu)I_L \tag{3}$$

$$S'_{H_h} = (1-p)(1-r)\Lambda - \rho_2 S_{H_h}\frac{S_{L_u} + S_{H_u}}{N} - \mu S_{H_h} + \gamma_2 I_H \tag{4}$$

$$S'_{H_u} = \rho_2 S_{H_h}\frac{S_{L_u} + S_{H_u}}{N} - (\alpha_2 + \mu)S_{H_u} \tag{5}$$

$$I'_H = (1-p)r\Lambda + \alpha_2 S_{H_u} - (\nu_2 + \gamma_2 + \mu)I_H \tag{6}$$

$$N = S_{L_h} + S_{L_u} + I_L + S_{H_h} + S_{H_u} + I_H \tag{7}$$

Equations (1) through (3) represent the dynamics of the population with low genetic predisposition to atherosclerosis. We assume that genetic predispositions are non-modifiable. Equations (4) through (6) describe the dynamics of the population with high genetically predisposition. The total population, $N$, is assumed to be locally asymptotically constant because the limit as $N$ approaches infinity, then $N$ becomes $\frac{\Lambda}{\mu}$ which is constant.

To calculate the reproductive number, we first find the Unhealthy Disease-Free Equilibrium (UDFE). We assume $r = 0$, therefore no individuals enter the model directly via the infected class, $I_H$. The UDFE is given by:

$$UDFE = (S_{L_h}{}^*, S_{L_u}{}^*, S_{H_h}{}^*, S_{H_u}{}^*, I_L{}^*, I_H{}^*) = \left(\frac{p\Lambda}{\mu}, 0, \frac{(1-p)\Lambda}{\mu}, 0, 0, 0\right).$$

The UDFE is locally asymptotically stable when $R_0 < 1$. For $r = 0$ we calculated the existence of an endemic equilibrium using the intermediate value theorem (see Appendix) and extended this result to the general case when $r > 0$.

$$R_0 = \frac{\rho_1 p}{\mu + \alpha_1} + \frac{\rho_2(1-p)}{\mu + \alpha_2}. \tag{8}$$

From analysis of the above model, we compute the basic reproductive number, $R_0$ (for detailed computation, see Appendix A), which only exists when $r = 0$. $R_0$ is the average number of secondary unhealthy individuals generated by a typical unhealthy individual. $\rho_1$ is the proportion of people that come into the system with low genetic predisposition to atherosclerosis and $(1-p)$ is the proportion of people that come into the system with high genetic predisposition to atherosclerosis. $\rho_i$ is the contact (transmission) rate and $\frac{1}{\mu+\alpha_i}$ is the average unhealthy ("infectious") period. $\frac{\rho_1 p}{\mu+\alpha_1}$ is the contribution to infection of the genetically low predisposed individuals and $\frac{\rho_2(1-p)}{\mu+\alpha_2}$ is the contribution of the genetically high predisposed individuals. Therefore, the model assumes that initially growth ($R_0$) is the result of two additive effects.

Table 1: Description of Parameters

| Parameters | Description |
|---|---|
| $\mu$ | natural death rate |
| $\rho_i$ | rate at which healthy susceptible become unhealthy |
| $\alpha_i$ | natural progression rate from unhealthy to diagnosed |
| $\gamma_i$ | recovery rate |
| $\nu_i$ | disease induced mortality |
| $p$ | fraction of population entering genetically low predisposed class |
| $r$ | fraction of new births with CVDs |
| $\Lambda$ | number of births per year |

## 4 Parameter Values

Using data from the American Heart Association's (AHA) *Heart Disease and Stroke Statistics- 2005 Update* on risk factors, prevalence, incidences, and deaths as a result of cardiovascular diseases we were able to determine some of the parameters in our model [21]. We acquire other statistics from The Center for Disease Control (CDC) [9], in particular the data needed to determine the birth rates ($\Lambda$) and the natural death rates ($\mu$) of the African American and Caucasian American populations. The population size, $N$, is obtained from the Census Bureau and is based on the 2000 census statistics and projections for the year 2002 [10].

According to the CDC, the life expectancy for African Americans is 71.4 years and for Caucasian Americans is 77.3 years. We use this data to determine the natural death rate ($\mu$) of each population.

$$\mu \approx \frac{1}{\text{Life Expectancy}}$$

The natural death rate for African Americans is 0.0140056 year$^{-1}$, and the life expectancy for Caucasian Americans is 0.0129366 year$^{-1}$.

The data on $p$ is not available, therefore we estimated the value of $p$ based on information that suggests 40% of the African American and 30% of the Caucasian American population naturally have high blood pressure, a condition directly correlated with CVD prevalence. We estimated that 40% of African American and 30% of Caucasian American newborns enter the system with a high genetic predisposition to CVDs ($S_{H_h}$) while all other individuals enter through the genetically low predisposed class ($S_{L_h}$). Thus, we let $p = 0.6$ for the African American population and $p = 0.7$ for the Caucasian American population. Some studies have found that a small percentage of the population will develop atherosclerosis even while leading a healthy lifestyle [8]. In our model, this percentage of the population, $\Lambda r(1 - p)$, goes directly into the infected class, $I_H$. Since this portion of

the population is small we estimate this percentage to be approximately 1% ($r \approx 0.01$).

Data from the AHA states that CVD prevalence is higher among African Americans than among Caucasian Americans [8]. These rates of progression within a given population from unhealthy to diagnosed classes must be consistent with this data. We define our parameters $\alpha_1$ and $\alpha_2$ as the rates at which individuals in $S_{L_u}$ and $S_{H_u}$ progress from unhealthy to infected, $I_L$ and $I_H$, respectively.

Because of differences in genetic predisposition, we assume that individuals in $S_{H_u}$ develop atherosclerosis at a faster rate than individual in $S_{L_u}$. Therefore, we assume that $\alpha_2 > \alpha_1$ and determine distinct progression rates for each population. We let $\alpha = \alpha_1 + \alpha_2$, and obtained the approximate value of $\alpha$ using the number of incidences of CVDs per year and the size of a given population, African American or Caucasian American in this case.

$$\alpha \approx \frac{\text{Number of individuals with CVD per year}}{\text{Total population}}$$

Based on statistical data our approximation of $\alpha$ represents the percentage of the population that develops CVDs. We use our approximation of $p$ when calculating the rate of progression from unhealthy to infected classes. By letting $\alpha_1 = (1 - p)\alpha$ and $\alpha_2 = p\alpha$, the condition that $\alpha_2 > \alpha_1$ is satisfied. Using the specific value $p$ to assign a value to each $\alpha_i$ gives consistency when comparing the values of $\alpha_1$ for African American ($\alpha_{1AA}$) and $\alpha_1$ for Caucasian American ($\alpha_{1CA}$). Also, it is apparent that $\alpha_{1AA} > \alpha_{1CA}$. The previous condition predicts a higher prevalence for CVDs among the African American population, which is consistent with prevalence statistics from the American Heart Association [8].

The disease induced death rate, $\nu$, is calculated for African Americans ($\nu_{AA}$) and Caucasian Americans ($\nu_{CA}$) using the total number of deaths due to CVDs per year from each population.

$$\nu \approx \frac{\text{Total CVD induced deaths per year}}{\text{Total population}}$$

Our calculations suggest that $\nu_{CA} > \nu_{AA}$. In fact, $\nu_{CA}$ is approximately ten times larger than $\nu_{AA}$. Our values agree with data from the AHA that states that disease induced deaths are nine times higher in Caucasian Americans than in African Americans. We assume that individuals with a higher genetic predisposition to developing a CVD have a higher probability of dying from that CVD than individuals with a lower genetic predisposition to developing the same CVD.

In determining $\gamma_i$, we consider a person as recovered once they undergo surgical procedures. The AHA reports a total number of successful surgeries for the entire US population. We used this value to calculate the recovery rate.

$$\gamma \approx \frac{\text{Total successful surgeries per year}}{\text{Total diagnosed cases}}$$

We let the recovery rate of the African American population equal to the recovery rate of the Caucasian American population, $\gamma_{AA} = \gamma_{CA}$. Therefore, we assume all populations have an equal recovery rate.

We summarize our parameter values from 1 in Table 2. The initial values can be found in Table 3.

Table 2: Parameter Values

| Parameters | African American | Caucasian Americans | References |
|---|---|---|---|
| $\mu$ (year$^{-1}$) | 0.014005602 | 0.012936611 | Census Bureau [10] |
| $\rho_i$ (year$^{-1}$) | $0 \leq \rho_i \leq 0.5$ | $0 \leq \rho_i \leq 0.5$ | |
| $\alpha_1$ (year$^{-1}$) | 0.0198048428 | 0.0018925509 | AHA [21] |
| $\alpha_2$ (year$^{-1}$) | 0.0297072642 | 0.0044159521 | AHA [21] |
| $\gamma_1$ (year$^{-1}$) | 0.0971897 | 0.0971897 | AHA [21] |
| $\gamma_2$ (year$^{-1}$) | 0.0971897 | 0.0971897 | AHA [21] |
| $\nu_1$ (year$^{-1}$) | 0.00105 | 0.0044 | AHA [21, 10] |
| $\nu_2$ (year$^{-1}$) | 0.00245 | 0.02716 | AHA [21, 10] |
| $p$ | 0.6 | 0.7 | AHA [21] |
| $r$ | 0.01 | 0.01 | AHA [21] |
| $\Lambda$ | 485409 | 2735583 | Census Bureau [10] |

Table 3: Initial Conditions

| Population | African Americans | Caucasian Americans |
|---|---|---|
| $N$ | 34658190 | 211460626 |
| $S_{L_h}$ | 20794913 | 148022437 |
| $S_{L_u}$ | 100000 | 100000 |
| $I_L$ | 0 | 0 |
| $S_{H_h}$ | 13863275 | 634381868 |
| $S_{H_u}$ | 100000 | 100000 |
| $I_H$ | 0 | 0 |

## 5    Numerical Simulations

We perform numerical simulations to illustrate how interactions between healthy and unhealthy individuals affect the overall dynamics of atherosclerosis. Based on data from the American Heart Association (AHA) we study African American and Caucasian American populations.
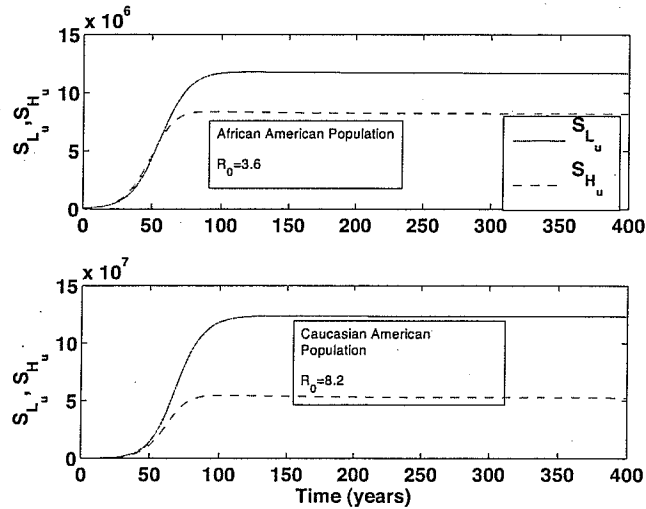
Figure 2: Low-risk and high-risk susceptibles (African American and Caucasian American Populations). Parameter values: $\rho_1 = 0.1$, $\rho_2 = 0.2$, $r = 0$. For the remaining parameter values and initial conditions, see Tables 2, and 3.

In Figure 2 we illustrate the existence of an endemic equilibrium. In this case, both populations increase rapidly at the same time and reach and endemic equilibrium. The percentage of the African American and Caucasian American Population that become low-risk unhealthy over time is approximately 33% and 61%, respectively. However, It is therefore expected that this population would account for a larger percentage of unhealthy individuals over time. The high-risk unhealthy is approximately the same for both populations (24%).

Figure 3 shows the number of individuals who have progressed to atherosclerosis. For the African American Population both the low-risk and high-risk individuals are approximately the same at 6% and the Caucasian American Population reaches an endemic equilibrium at approximately 1% (low-risk) and 0.8 (high-risk). Progression to atherosclerosis is slow and highly dependent on an individual's behavior.

When $\rho_i$ is small enough to make $R_0 < 1$, we have that the number of African American unhealthy individuals decreases to zero. In the case of the Caucasian American population, it takes longer for the population to decrease to zero. The number of high-risk unhealthy individuals decreases more rapidly than the low-risk population (see Figure 4).

Figure 5 illustrates the case when $R_0$ is reduced by decreasing $\rho_i$ in both populations in question. Although the Caucasian American population has very low levels of endemicity the population is much larger than the African
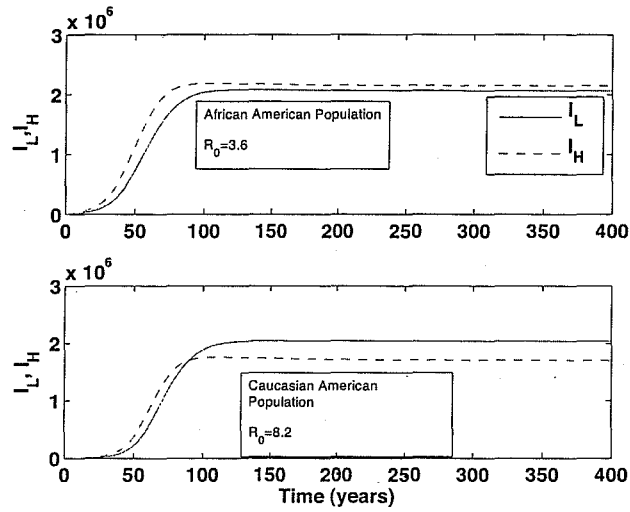
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Figure 3: Low-risk and high-risk infected individuals (African American and Caucasian American Populations). Parameter values: $\rho_1 = 0.1$, $\rho_2 = 0.2$, $r = 0$. For the remaining parameter values and initial conditions, see Tables 2, and 3.
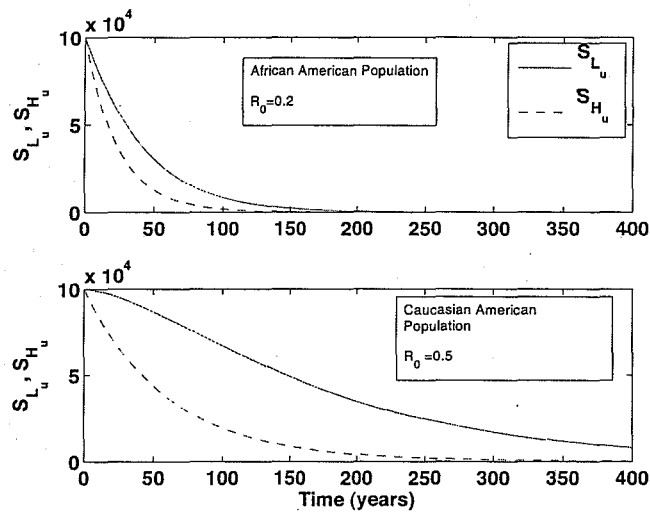


Figure 4: Low-risk and high-risk susceptibles (African American Population).Parameter values: $\rho_1 = 0.01$, $\rho_2 = 0.002$, $r = 0$. (Caucasian American Population). Parameter values: $\rho_1 = 0.01$, $\rho_2 = 0.001$, $r = 0$
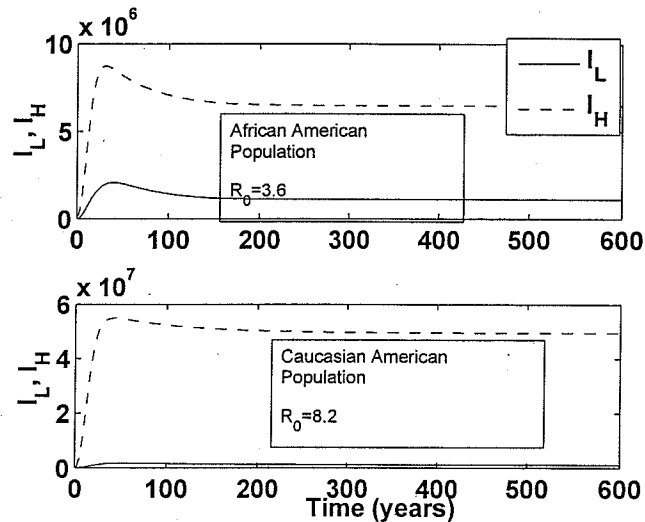
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Figure 5: Low-risk and high-risk infected individuals when $r = 0.01$. (African American and Caucasian American Populations). Parameter values: $\rho_1 = 0.1$, $\rho_2 = 0.2$, $r = 0.01$. For the remaining parameter values and initial conditions, see Tables 2, and 3.

American population. In Figure 5 we show that even by having $r > 0$ there is little change in the overall dynamics of the system. The total population that has progressed to atherosclerosis is approximately $I_L = 5.7\%$ and $I_H = 3.3\%$ for the African American population. For the Caucasian American population it is approximately $I_L = 0.8\%$ and $I_H = 0.6\%$.

## 6   Different Health Care: An Extended Model

We extend our model to study the possible effects of two different levels of access to health care. Some individuals who encounter cardiovascular complications may seek immediate medical attention at hospitals that specialize or are capable of treating their condition. We assume these people have an adequate health care provider and are well informed about the type of treatments for their conditions. However, individuals with economic constraints may not have an adequate health care provider or may be misinformed about the treatments available for their conditions and, upon an incidence of the above mentioned, may seek medical attention at hospitals that are not adequate to treat their condition. This can happen when the health care provider only covers costs at a specific hospital or when the individual does not know which hospital can treat their condition.

Because not all individuals receive proper treatment, we add two recovery classes, $R_L$ and $R_H$, which allow for the possibility that a percentage of those who receive treatment will relapse due to improper medical treatment. All
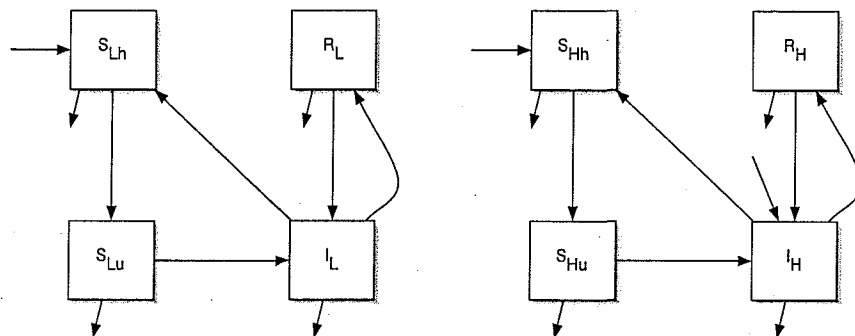
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Figure 6: Caricature of the extended model. $R_L$ and $R_H$, represent the recovered classes for the low and high genetic predisposition, respectively. $\eta_i$ (flow from $I_i$ to $R_i$) is the recovery rate and omega ($\omega$) (flow from $R_i$ to $I_i$) the relapse rate.

individuals that receive improper treatment can recover at rate $\eta_i$ and may relapse at rate $\omega$.
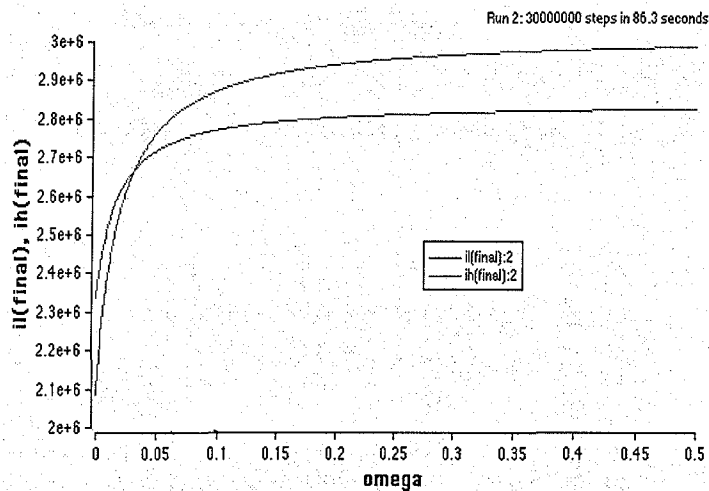


Figure 7: Equilibrium values of $I_L$ and $I_H$ for various values of omega ($\omega$).

We assume the recovery rates $\gamma_1$ and $\gamma_2$ are much larger than the rates at which people move to the $R$ classes, $\eta_1$ and $\eta_2$, respectively. We assume that the population that receives proper treatment and recovers either has an adequate health care provider or seeks medical attention at hospitals that will treat their conditions adequately.
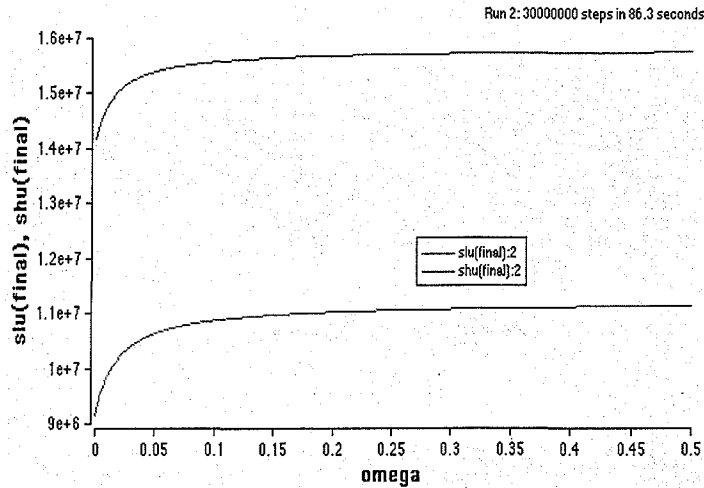
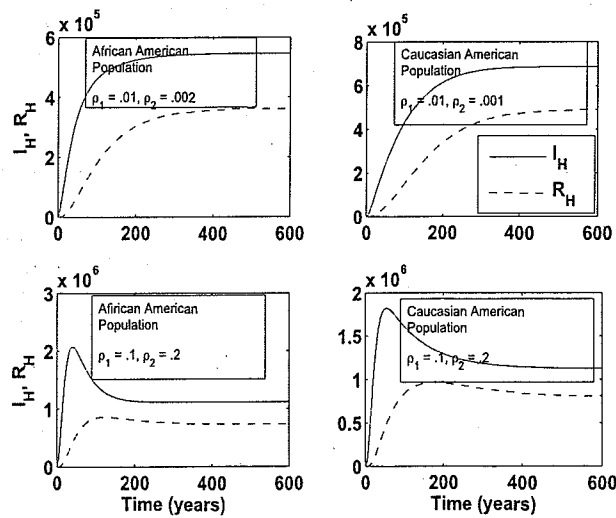Figure 8: Equilibrium values of $S_{L_u}$ and $S_{H_u}$ for various values of omega ($\omega$).



Figure 9: In this graph, $r > 0$ and we vary $\rho_i$ where $r > 0$ for both the African American and Caucasian American population. Parameters: (African American) $\eta_1 = 0.01$, $\eta_2 = 0.02$, and $\omega_1 = \omega_2 = 0.001$. The low-risk and high-risk infected individuals of each population reach an endemic equilibrium (with 3.4% and 0.6% of the population, respectively) faster when $\rho_i$ is large. In contrast, when $\rho_i$ is small it takes longer to reach and endemic equilibrium (1.7% and 0.32%, respectively) but there are less individuals in the $I$ classes.

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$$S'_{L_h} = p\Lambda - \rho_1 S_{L_h} \frac{S_{L_u} + S_{H_u}}{N} + \gamma_1 I_L - \mu S_{L_h} \tag{9}$$

$$S'_{L_u} = \rho_1 S_{L_h} \frac{S_{L_u} + S_{H_u}}{N} - S_{L_u}(\alpha_1 + \mu) \tag{10}$$

$$I'_L = \alpha_1 S_{L_u} + \omega_1 R_L - (\nu_1 + \gamma_1 + \eta_1 + \mu)I_L \tag{11}$$

$$R'_L = \eta_1 I_L - (\omega_1 + \nu)R_L \tag{12}$$

$$S'_{H_h} = (1-p)(1-r)\Lambda - \rho_2 S_{H_h} \frac{S_{L_u} + S_{H_u}}{N} - \mu S_{H_h} + \gamma_2 I_H \tag{13}$$

$$S'_{H_u} = \rho_2 S_{H_h} \frac{S_{L_u} + S_{H_u}}{N} - S_{H_u}(\alpha_2 + \mu \tag{14}$$

$$I'_H = (1-p)r\Lambda + \alpha_2 S_{H_u} + \omega_2 R_H - (\nu_2 + \gamma_2 + \eta_2 + \mu)I_H \tag{15}$$

$$R'_H = \eta_2 I_H - (\omega_2 + \nu)R_H \tag{16}$$

$$N = S_{L_h} + S_{L_u} + I_L + R_L + S_{H_h} + S_{H_u} + I_H + R_H \tag{17}$$

In Figure 9 we illustrate the dynamics of the system when $r = 0.01$. In the African American population $I_H = 3.3\%$ and $R_H = 2.4\%$ while in the Caucasian American population $I_H = 1\%$ and $R_H = 1.1\%$. Both populations reach an endemic equilibrium at approximately the same time ($\approx 200$ years). However, in the Caucasian American population the number of recovered ($R_H$) reaches a higher endemic state than the number of individuals with atherosclerosis. This can be the result of individuals with higher risks of progressing to atherosclerosis may seek better health ($\eta_2 > \eta_1$).

Our results suggest that the overall behavior of the system does not change significantly when the $R$ classes are added. This is indicates that the dynamics of the population can be equally described by the model without recovered classes ($R_L$ and $R_H$).

Varying $\omega$ results in changing the rate at which individuals in the $R$ classes relapse to the infected class. As stated above, when $\omega$ is large the population behaves similar as to when there are no $R$ classes. When $\omega = 0$ relapse does not occur, people that recover to the $R$ classes are no longer susceptible to the diseases and will remain in $R$ until they die of natural causes. The size of the infected classes will decrease significantly because those that recover to $R$ can never return to $I$. Figures 7, 8 show the dynamics of the system when $\omega[0, 0.3]$.

Further work should include determining accurate values for all recovery rates taking into account socioeconomics status, as well as, awareness of available treatments for CVDs. A more accurate relapse rate would also help in determining the equilibrium behavior of this system.
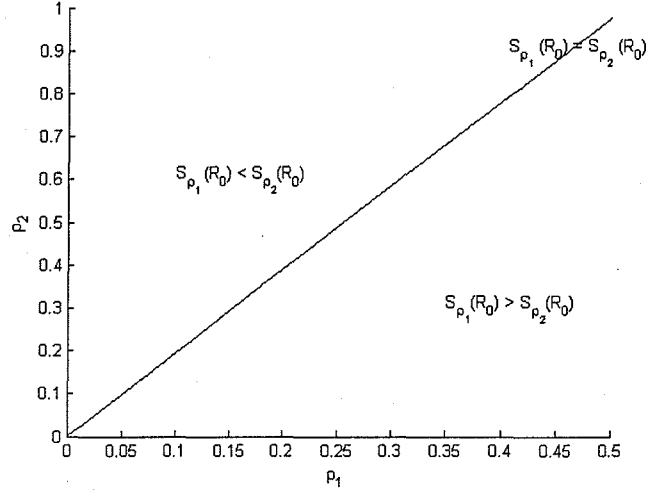
Figure 10: Sensitivity Analysis of $R_0$ in terms of $\rho_1$ and $\rho_2$.

## 7    Sensitivity and Uncertainty Analysis

### 7.1    Sensitivity Analysis

We perform a sensitivity analysis on $R_0$ by finding the normalized forward sensitivity index $S_p := \frac{\partial J}{\partial p}\frac{p}{J}$ where $J$ is the the functional and $p$ is the parameter. First, we find the sensitivity indices of the contact rates, $\rho_1$ and $\rho_2$.

$$S_{\rho_1}(R_0) = \frac{\rho_1}{R_0}\frac{\partial R_0}{\partial \rho_1} = \frac{\rho_1}{R_0}\frac{p}{(\mu + \alpha_1)} = \frac{\rho_1 p}{R_0(\mu + \alpha_1)}$$

$$S_{\rho_2}(R_0) = \frac{\rho_2}{R_0}\frac{\partial R_0}{\partial \rho_2} = \frac{\rho_2}{R_0}\frac{1-p}{(\mu + \alpha_2)} = \frac{\rho_2(1-p)}{R_0(\mu + \alpha_2)}$$

In Figure 10, we graph $\rho_2 = \frac{\rho_1 p(\mu + \alpha_2)}{(\mu + \alpha_1)(1-p)}$ to show conditionally how $\rho_1$ and $\rho_2$ affect $R_0$. From this graph we are able to find pairings of $\rho_1$ and $\rho_2$ that will show changes in the unhealthy population in our numerical simulations that will be discussed in Section 7.

### 7.2    Uncertainty Analysis

We perform uncertainty analysis on $R_0$ to analyze the accuracy of our result and to determine whether or not there is a significant uncertainty in the parameters. Using Monte Carlo Simulations with a sample size of 1000 and over a uniform distribution, as shown in table 4, we determine that there is a high probability that $R_0 > 1$ with a small standard error (SE)
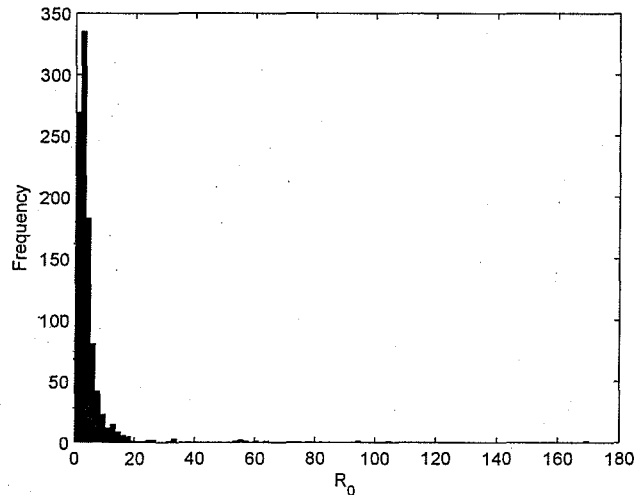
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Figure 11: Distribution of $R_0$.

(see Figure 11). Since there is a high probability that $R_0 > 1$ this implies there is a low probability that a UDFE will occur. We also find that both $\rho_1$ and $\rho_2$ contribute to any uncertainty of $R_0$ based on the sensitivity analysis of $R_0$. Results will be discussed in Section 7.

## 8    Conclusion and Discussion

We calculated the reproductive number, $R_0$, and performed an uncertainty and sensitivity analysis.

We focus on two specific populations, African American and Caucasian American for numerical analysis.

Interactions between healthy and unhealthy classes are modeled by non linear differential equations. Non-linearity exists between the low genetically predisposed healthy and unhealthy classes, as well as between the high genetically predisposed heathy and unhealthy classes. These non-linear terms account for the interactions that take place between all healthy and unhealthy individuals in a given population regardless of ones genetic predisposition to developing CVDs.

As the number of contacts between healthy and unhealthy classes increase, the unhealthy population increases. When we increase $\rho_1$ and fix $\rho_2$ the population of unhealthy individuals with low genetic predisposition increases, causing the number of unhealthy individuals with high genetic predisposition to increase as well. We find that when we increase $\rho_1$ the healthy classes reach endemic equilibrium faster and with a lower population, allowing the infected classes to become larger over a shorter amount

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| Realization | $Mean(R_0)$ | $std(R_0)$ | $p(R_0 > 1)$ |
|:---:|:---:|:---:|:---:|
| 1 | 4.155 | 5.298 | 0.876 |
| 2 | 4.037 | 5.552 | 0.882 |
| 3 | 3.969 | 6.308 | 0.885 |
| 4 | 4.090 | 4.880 | 0.910 |
| 5 | 4.085 | 5.401 | 0.877 |
| 6 | 4.477 | 7.433 | 0.902 |
| 7 | 4.305 | 7.199 | 0.879 |
| 8 | 3.941 | 4.514 | 0.890 |
| 9 | 3.967 | 4.959 | 0.875 |
| 10 | 4.553 | 8.837 | 0.876 |
| mean | 4.1579 | 6.0380 | .8852 |
| se | 0.0686 | 0.4374 | 0.0038 |
| cv | 0.0522 | 0.2291 | 0.0136 |

Table 4: We used a sample size of 1000 for each realization.

of time. Varying $\rho_2$ and holding $\rho_1$ gives similar results.

Our results suggests that some fraction of the population with high genetic predisposition will develop atherosclerosis regardless of how healthy life they lead. Thus, $r$ is a genetic factor.

To eradicate CVDs, the ideal condition is $R_0 < 1$. Decreasing $\rho_1$ and $\rho_2$ and increasing $\alpha_1$ and $\alpha_2$ reduces the value of $R$. We conclude that the best strategy for reducing the number of deaths caused by CVDs is to decrease the rate at which healthy individuals adopt unhealthy lifestyles, and by allowing unhealthy individuals to develop CVDs naturally. We can decrease the probability that the healthy population will adopt an unhealthy lifestyle by decreasing the probability that an interaction between a healthy and unhealthy individual will be lifestyle changing, that is, by decreasing $\rho_1$ and $\rho_2$. Decreasing $\rho_1$ and $\rho_2$ results in a decrease of the prevalence of CVDs because less individuals are susceptible to atherosclerosis and thus less individuals will develop or die of this condition. By maintaining good exercise, diet habits, and by educating society about the risks and dangers of CVDs, we may be able to accomplish this.

The values of $\alpha_1$ and $\alpha_2$ should not be altered. Decreasing $\alpha_1$ and $\alpha_2$ decreases the rate at which unhealthy individuals develop the disease, but it does not significantly decrease the number of individuals that develop it. Thus, decreasing $\alpha_1$ and $\alpha_2$ is counterproductive to reducing the number of yearly deaths due to CVDs because this results in increasing the average age at which individuals develop the disease. According to the American Heart Association, the older an individual gets, the more likely they are to die due to a CVD. Therefore, increasing the average age at which individuals develop the disease will increase the number of deaths a year that are caused

by CVDs because a larger percent of new incidences will be experienced by older people.

A better strategy in battling CVDs is to allow individuals that are already leading unhealthy lifestyles to develop the disease at the earliest age possible; this is equivalent to increasing the $\alpha_i$ . As a result individuals can undergo medical treatment and possibly recover to a susceptible class. Individuals of a younger age have a lower probability of dying due to a CVD and are more likely to recover from surgery.

The dynamics of CVD development are similar for the African American and Caucasian American populations. Respective populations sizes and the percentage of new births that are born with a high genetic predisposition for each population account for the differences in equilibrium values; however, the dynamics of either population are not affected. We assume both populations interact similarly; that is, we assume that $\rho_1$ and $\rho_2$ are the same for both populations, respectively, and they can be varied in a similar fashion.

Preventative medicine, when applied to the unhealthy classes, is counterproductive to battling CVDs because it delays the classes' progression to diagnosis causing the individuals to remain longer in the unhealthy class. As a result, the unhealthy classes' probability of death due to disease increases. Ideally we would like to increase $\alpha_1$ and $\alpha_2$; however, it is not biologically possible. We conclude that it is best to leave these parameters unchanged so that more individuals can experience CVD related complications early in life and have a higher probability of successfully recovering with the opportunity to lead a healthier life thereafter. However, increasing CVD awareness (education) and health consciousness are the best tools available in decreasing CVD prevalence because this effectively decreases the number of individuals that become unhealthy through social interactions, that is, by decreasing $\rho_1$ and $\rho_2$.

## 9 Acknowledgments

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## 10 Appendix

### Calculating $R_0$

Note: at the UDFE $N = \frac{\Lambda}{\mu}$. The Jacobian at UDFE is

$$J_0 = \begin{pmatrix} -\mu & -\rho_1 p & 0 & -\rho_1 p & \gamma & 0 \\ 0 & \rho_1 p - \mu - \alpha_1 & 0 & \rho_1 p & 0 & 0 \\ 0 & -\rho_2(1-p) & -\mu & \rho_2(1-p) & 0 & \gamma \\ 0 & \rho_2(1-p) & 0 & \rho_2(1-p) - \mu - \alpha_2 & 0 & 0 \\ 0 & \alpha_1 & 0 & 0 & -(\nu_1 + \mu + \gamma_1) & 0 \\ 0 & 0 & 0 & \alpha_2 & 0 & -(\nu_2 + \mu + \gamma_2) \end{pmatrix}$$

We can eliminate the first row and column because $\lambda_1 = -\mu$ is an eigenvalue.

$$J_1 = \begin{pmatrix} \rho_1 p - \mu - \alpha_1 & 0 & \rho_1 p & 0 & 0 \\ -\rho_2(1-p) & -\mu & \rho_2(1-p) & 0 & \gamma_2 \\ \rho_2(1-p) & 0 & \rho_2(1-p) - \mu - \alpha_2 & 0 & 0 \\ \alpha_1 & 0 & 0 & -(\nu_1 + \mu + \gamma_1) & 0 \\ 0 & 0 & \alpha_2 & 0 & -(\nu_2 + \mu + \gamma_2) \end{pmatrix}$$

Since $\lambda_2 = -\nu_1$, we can eliminate the second row and second column.

$$J_2 = \begin{pmatrix} \rho_1 p - \mu - \alpha_1 & \rho_1 p & 0 & 0 \\ \rho_2(1-p) & \rho_2(1-p) - \mu - \alpha_2 & 0 & 0 \\ \alpha_1 & 0 & -(\nu_1 + \mu + \gamma_1) & 0 \\ 0 & \alpha_2 & 0 & -(\nu_2 + \mu + \gamma_2) \end{pmatrix}$$

Now, $\lambda_3 = -(\nu_1 + \mu + \gamma_1)$, we can reduce the Jacobian again by eliminating the third row and the third column.

$$J_3 = \begin{pmatrix} \rho_1 p - \mu - \alpha_1 & \rho_1 p & 0 \\ \rho_2(1-p) & \rho_2(1-p) - \mu - \alpha_2 & 0 \\ 0 & \alpha_2 & -(\nu_2 + \mu + \gamma_2) \end{pmatrix}$$

Since $\lambda_4 = -(\nu_2 + \mu + \gamma_2)$ we can eliminate the third row and third column of the above matrix and we reduce the Jacobian to a $2 \times 2$ matrix:

$$J_4 = \begin{pmatrix} \rho_1 p - \mu - \alpha_1 & \rho_1 p \\ \rho_2(1-p) & \rho_2(1-p) - \mu - \alpha_2 \end{pmatrix}$$

We were able to calculate $R_0$ using the next generation operator for $J = M - D$, when $M$ is a non-negative matrix and $D$ is a diagonal matrix.

$$M - D = \begin{pmatrix} \rho_1 p & \rho_1 p \\ \rho_2(1-p) & \rho_2(1-p) \end{pmatrix} - \begin{pmatrix} \alpha_1 + \mu & 0 \\ 0 & \mu + \alpha_2 \end{pmatrix}$$

We can calculate $D^{-1}$,

$$D^{-1} = \begin{pmatrix} \frac{1}{\alpha_1 + \mu} & 0 \\ 0 & \frac{1}{\mu + \alpha_2} \end{pmatrix}$$

Therefore, we can calculate $R_0 = MD^{-1}$.

$$MD^{-1} = \begin{pmatrix} \rho_1 p & \rho_1 p \\ \rho_2(1-p) & \rho_2(1-p) \end{pmatrix} \begin{pmatrix} \frac{1}{\alpha_1 + \mu} & 0 \\ 0 & \frac{1}{\mu + \alpha_2} \end{pmatrix} = \begin{pmatrix} \frac{\rho_1 p}{\alpha_1 + \mu} & \frac{\rho_1 p}{\alpha_2 + \mu} \\ \frac{\rho_2(1-p)}{\alpha_1 + \mu} & \frac{\rho_2(1-p)}{\alpha_2 + \mu} \end{pmatrix}$$

We solve for the two final eigenvalues and find the dominant eigenvalue:

$$R_0 = \frac{\rho_1 p}{\alpha_1 + \mu} + \frac{\rho_2(1-p)}{\alpha_2 + \mu}$$

**Endemic Equilibrium**

When $r = 0$, the solutions of the following system are equilibrium points.

$$
\begin{align}
0 &= p\Lambda - \rho_1 S_{L_h} \frac{S_{L_u} + S_{H_u}}{N} + \gamma_1 I_L - \mu S_{L_h} \tag{18} \\
0 &= \rho_1 S_{L_h} \frac{S_{L_u} + S_{H_u}}{N} - \alpha_1 S_{L_u} - \mu S_{L_u} \tag{19} \\
0 &= \alpha_1 S_{L_u} - (\nu_1 + \gamma_1 + \mu) I_L \tag{20} \\
0 &= (1-p)(1-r)\Lambda - \rho_2 S_{H_h} \frac{S_{L_u} + S_{H_u}}{N} - \mu S_{H_h} + \gamma_2 I_H \tag{21} \\
0 &= \rho_2 H_h \frac{S_{L_u} + S_{H_u}}{N} - \alpha_2 S_{H_u} - \mu S_{H_u} \tag{22} \\
0 &= (1-p)r\Lambda + \alpha_2 S_{H_u} - (\nu_2 + \gamma_2 + \mu) I_H \tag{23} \\
0 &= S_{L_h} + S_{L_u} + I_L + S_{H_h} + S_{H_u} + I_H \tag{24}
\end{align}
$$

Adding equations (18) through (24), we get

$$\Lambda + \mu N - (\nu_1 I_L + \nu_2 I_H) = 0.$$

Solving this equation for $N$ gives

$$N = \Lambda - \frac{\nu_1 I_L + \nu_2 I_H}{\mu} := N(I_L, I_H)$$