

Optimal Control of Myocardial Infarction due to Diabetes

A. I. Adekunle¹ and O. Olotu

Department of Mathematical Sciences, Federal University of Technology,
P.M.B 704 Akure, Ondo State, Nigeria

Abstract

Optimal control theory is applied to a system of ordinary differential equations modeling myocardial infarction due to diabetes epidemiology model. For this model, controls representing prevention and recovery are incorporated to reduce the population with myocardial infarction via the application of the Pontryagin's Maximum Principle of optimal control theory. The optimal controls are characterized in terms of the optimality system, which is solved numerically for several scenarios.

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1 Introduction

Diabetes Mellitus(DM) is a chronic non-communicable disease widespread around the world. It refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM exist and are caused by a complex interaction of genetics and environmental factors. Depending on the etiology of the DM, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production[1]. A global epidemic of diabetes is expected[2].

Myocardial infarction (MI) or acute myocardial infarction (AMI), commonly known as a heart attack, results from the interruption of blood supply to a part of the heart, causing heart cells to die. Immediately after an acute coronary occlusion, blood flow ceases in coronary vessels beyond the occlusion except for small amount of collateral flow from surrounding vessels. The area of muscle that has either zero flow or so little flow that it cannot sustain cardiac muscle function is said to be infarcted. The overall process is called a myocardial infarction. We must mention that if there is even as much as 15 to 30 per cent of normal resting coronary blood flow, the muscle will not die. However for blood flow is less than this, the muscle does die.[3].

Diabetes has been confirmed to be an independent risk factor for the occurrence of coronary disease. The link between diabetes and coronary diseases has been known for some 70 years[4]. A risk for diabetics to suffer from coronary diseases is 2-4 times higher than in nondiabetics[5]. Alajbegovic et al[6] shows that MI is prevalent and more significant in diabetics patient than nondiabetics patients. Control program for myocardial has been attributable to efforts in primary

¹Corresponding Author. Email: kunle102@yahoo.com

prevention as well as improved therapies for myocardial infarction. Most primary-prevention efforts have focused on the major modifiable determinants of risk: cigarette smoking, an elevated blood cholesterol level, hypertension, and a sedentary lifestyle. In addition, the modification of other known coronary risk factors such as obesity and diabetes has been studied. Attention has most recently been directed toward the possible benefits of estrogen-replacement therapy in postmenopausal women, moderate alcohol consumption, and low-dose aspirin prophylaxis in apparently healthy people[7]. Furthermore, a quality control programme methodology, showed that the chronology of MI management could be improved by appropriate interventions and monitoring of intervention times[8].

Some past epidemiological model of myocardial infarction have considered the prevalence and significant of the disease based on Chi-square test[6] and stability analysis of the model[9]. The effectiveness of the diffusion of data, implementation of correctives measures and updated protocols has been used in reducing time to reperfusion in myocardial infarction (MI) management in the out-of-hospital setting[8]. In particular, an interesting literature has been devoted to studies collecting, analyzing and validating data concerning diabetes populations. A variety of mathematical models, statistical methods and computer algorithms have been proposed in order to understand different aspects of diabetes such as: glucose-insulin dynamics, epidemiology of diabetes and its complications, cost of diabetes and cost-effectiveness of strategies dealing with diabetes [9]. However, these models did not account for time-dependent control strategies since their discussion are based on prevalence of the MI on diabetic patients. Time dependent control strategies have been studied for Tuberculosis models (see [10] and [11]). Both approaches of studying control strategies produce valuable results which can be used to design control programs. Depending on a chosen goal(goal) various objective criteria may be developed.

The numbers of diabetic patients are increasing very fast all over the world, because of that, in this paper we consider(time dependent) optimal control strategies for prevention and recovery from myocardial infarction on diabetic patients for myocardial infarction due to diabetes epidemiology model developed by Khajehnasiri et al in [9]. Introduced into the model are control mechanisms representing prevention and recovery for individual diabetic patient with or without myocardial infarction.

The paper is organized as follows: Section 2 describes the myocardial infarction due to diabetes epidemiology model with control terms. Our objective functional is also introduced in this section. The analysis of the optimal controls is given in Section 3. Section 4 includes some numerical studies of the optimal controls and discusses our result.

2 Materials and Methods

The myocardial infarction recovery model from Khajehnasiri et. al.[9] divides the diabetes human population ($N(t)$) into the following sub-groups: diabetes individuals($D_{MI}(t)$), diabetes individuals that have myocardial infarction($M_{MI}(t)$) and those with diabetes and have recovered from myocardial infarction ($R_{MI}(t)$). Thus, the total variable diabetic population size at time t is given by,

$$N(t) = D_{MI}(t) + M_{MI}(t) + R_{MI}(t).$$

It is assumed that diabetic patients are recruited into the population at per capita rate Λ . The model parameters incorporated are μ (the natural mortality rate) and λ (the probability of

diabetic person having myocardial infarction). Hence,

$$\frac{dD_{MI}(t)}{dt} = \Lambda - \lambda D_{MI} - \mu D_{MI}.$$

The population of myocardial infarcted individuals is generated following a diabetic patient having myocardial infarction at the rate λ . This population is decreased by death due to myocardial infarction, recovery, patients who become severely disabled and which disability cannot be cured, and natural mortality at the rates δ , α , ν , μ , respectively. Hence,

$$\frac{dM_{MI}(t)}{dt} = \lambda D_{MI}(t) - \delta M_{MI}(t) - \alpha M_{MI}(t) - \nu M_{MI}(t) - \mu M_{MI}(t).$$

Finally, the recovered population is increased by myocardial infarction patients who recovered at the rate α and decreases by the natural mortality at the rate μ . Thus,

$$\frac{dR_{MI}(t)}{dt} = \alpha M_{MI} - \mu R_{MI}.$$

In summary, the model system in [9] is given as:

$$\frac{dD_{MI}(t)}{dt} = \Lambda - \lambda D_{MI} - \mu D_{MI}, \quad (2.1)$$

$$\frac{dM_{MI}(t)}{dt} = \lambda D_{MI} - \delta M_{MI} - \alpha M_{MI} - \nu M_{MI} - \mu M_{MI}, \quad (2.2)$$

$$\frac{dR_{MI}(t)}{dt} = \alpha M_{MI} - \mu R_{MI}. \quad (2.3)$$

According to Alajbegovic et al [6] recovered patients can relapse and have myocardial infarction. Assuming a relapse rate σ , then the model (2.1)-(2.3) becomes

$$\frac{dD_{MI}(t)}{dt} = \Lambda - \lambda D_{MI} - \mu D_{MI}, \quad (2.4)$$

$$\frac{dM_{MI}(t)}{dt} = \lambda D_{MI} + \sigma R_{MI} - \delta M_{MI} - \alpha M_{MI} - \nu M_{MI} - \mu M_{MI}, \quad (2.5)$$

$$\frac{dR_{MI}(t)}{dt} = \alpha M_{MI} - \sigma R_{MI} - \mu R_{MI}. \quad (2.6)$$

Hence, introducing the controls representing the level of efforts on prevention and recovery, the model (2.4)-(2.6) becomes

$$\frac{dD_{MI}(t)}{dt} = \Lambda - \lambda(1 - u_1(t))D_{MI} - \mu D_{MI}, \quad (2.7)$$

$$\frac{dM_{MI}(t)}{dt} = \lambda(1 - u_1(t))D_{MI} + \sigma(1 - u_1(t))R_{MI} - (\delta + \alpha u_2(t))M_{MI} - (\nu + \mu)M_{MI}, \quad (2.8)$$

$$\frac{dR_{MI}(t)}{dt} = \alpha u_2(t)M_{MI} - \sigma(1 - u_1(t))R_{MI} - \mu R_{MI}. \quad (2.9)$$

Where $D_{MI}(0)$, $M_{MI}(0)$, $R_{MI}(0)$ are given and the definitions of above model parameters are listed in Table 2.1. The control functions, $u_1(t)$ and $u_2(t)$ are bounded, Lebesgue integrable functions. The control, $(1 - u_1(t))$, represents the effort on prevention of diabetic patient having myocardial infarction to reduce the number of diabetic individuals that may develop myocardial infarction. While the control $u_2(t)$ is the effort on recovery from myocardial infarction to increase

the number of recovered individuals.

Parameter	Description	Baseline value	Reference
Λ	Recruitment rate	0.1964	[6]
μ	Natural death rate	0.7	[9]
δ	Mortality rate due to myocardial infarction	0.04	[9]
α	Recovery rate	0.2	[9]
ν	Rate at which diabetic patients with MI become severely disabled	0.04	[9]
λ	Probability of a diabetic person having myocardial infarction	0.01 – 0.7	[9]
σ	Modification parameter	0.9	assumed

Table 2.1: Description of Parameters of the Model (2.7)-(2.9).

Our objective functional to be minimized is

$$J(u_1, u_2) = \min_{u_1, u_2} \int_0^{t_f} (A_1 M_{MI} + B_1 u_1^2 + B_2 u_2^2) dt \quad (2.10)$$

where we want to minimize the diabetic myocardial infarction group while also keeping the cost of prevention and recovery low. We assume that the cost of prevention and cost of recovery are nonlinear and take quadratic form here. The coefficients A_1, B_1, B_2 are balancing cost factors due to scales and importance of the four parts of the objective function and t_f is the final time. We seek to find an optimal control pair, u_1^* and u_2^* such that

$$J(u_1^*, u_2^*) = \min\{J(u_1, u_2) | u_1, u_2 \in \mathcal{U}\} \quad (2.11)$$

where $\mathcal{U} = \{(u_1(t), u_2(t)) \in L^2(0, t_f) | a_i \leq (u_1(t), u_2(t)) \leq b_i, i = 1, 2, t \in [0, t_f]\}$ is the control set.

3 Results

The necessary conditions that an optimal control pair must satisfy come from Pontryagin’s Maximum Principle[12]. This principle converts (2.7)-(2.9) and (2.10) into a problem of minimizing pointwise a Hamiltonian, \mathcal{H} , with respect to u_1 and u_2 :

$$\mathcal{H} = A_1 M_{MI} + B_1 u_1^2 + B_2 u_2^2 + \sum_{i=1}^{i=3} \lambda_i g_i \quad (3.1)$$

where g_i is the right hand side of the differential equation (2.7)-(2.9), of the i th state variable. By applying Pontryagin’s Maximum Principle[12] and the existence result for the control pairs from [13], we obtain

Theorem 1. *There exists an optimal control pair u_1^*, u_2^* and corresponding solution, D_{MI}^*, M_{MI}^* and R_{MI}^* , that minimizes $J(u_1, u_2)$ over \mathcal{U} . Furthermore, there exists adjoint variables $\lambda_1 = \lambda_{D_{MI}}, \lambda_2 = \lambda_{M_{MI}}, \lambda_3 = \lambda_{R_{MI}}$ satisfying*

$$\frac{d\lambda_{D_{MI}}}{dt} = \lambda(1 - u_1)\lambda_{D_{MI}} + \mu\lambda_{D_{MI}} - \lambda(1 - u_1)\lambda_{M_{MI}}, \quad (3.2)$$

$$\frac{d\lambda_{M_{MI}}}{dt} = -A_1 + (\delta + \alpha u_2 + \nu + \mu)\lambda_{M_{MI}} - \alpha u_2 \lambda_{R_{MI}}, \quad (3.3)$$

$$\frac{d\lambda_{R_{MI}}}{dt} = -\sigma(1 - u_1)\lambda_{M_{MI}} + \sigma(1 - u_1)\lambda_{R_{MI}} + \mu\lambda_{R_{MI}}, \quad (3.4)$$

with transversality conditions

$$\lambda_{DMI}(t_f) = 0, \quad \lambda_{MMI}(t_f) = 0, \quad \lambda_{RMI}(t_f) = 0, \quad (3.5)$$

and $N^* = D_{MI}^* + M_{MI}^* + R_{MI}^*$.

The following characterizations hold

$$u_1^* = \min \left\{ b_1, \max \left[a_1, \frac{\sigma R_{MI}(\lambda_{MMI} - \lambda_{RMI}) - \lambda_{DMI}(\lambda_{DMI} + \lambda_{MMI})}{2B_1} \right] \right\} \quad (3.6)$$

and

$$u_2^* = \min \left\{ b_2, \max \left[a_2, \frac{\alpha M_{MI}(\lambda_{MMI} - \lambda_{RMI})}{2B_2} \right] \right\} \quad (3.7)$$

Proof. Corollary 4.1 of [13] gives the existence of an optimal control pair due to the convexity of integrand of J with respect to (u_1, u_2) , a priori boundedness of the state solutions, and the Lipschitz property of the state system with respect to the state variables. Applying Pontryagin's Maximum Principle, we obtain

$$\begin{aligned} \frac{d\lambda_{DMI}}{dt} &= -\frac{\partial H}{\partial D_{MI}}, \lambda_{DMI}(t_f) = 0, \\ \frac{d\lambda_{MMI}}{dt} &= -\frac{\partial H}{\partial M_{MI}}, \lambda_{MMI}(t_f) = 0, \\ \frac{d\lambda_{RMI}}{dt} &= -\frac{\partial H}{\partial R_{MI}}, \lambda_{RMI}(t_f) = 0, \end{aligned}$$

evaluated at the optimal control pair and corresponding states, which results in the stated adjoint system (3.2)-(3.4). By considering the optimality conditions,

$$\frac{\partial H}{\partial u_1} = 0, \quad \frac{\partial H}{\partial u_2} = 0$$

and solving for u_1^* , u_2^* subject to the constraints, the characterizations(3.6) and (3.7) can be derived. \square

Next, we discuss the numerical solutions of the optimality system and the corresponding optimal control pairs, the parameters choices, and the interpretations from various cases.

4 Discussion

In this section, we study numerically an optimal control of myocardial infarction strategy of our myocardial infarction diabetes model. The optimal control strategy is obtained by solving the optimality system, consisting the state equations (2.7)-(2.9) and adjoint equations (3.2)-(3.4), using the parameters in Table 2.1 and initial conditions: $D_{MI}(0) = 2000$, $M_{MI}(0) = 500$, $R_{MI}(0) = 0$ and final time(t_f) is 20 years . All computations were performed in the MATLAB environment, Version 7.10.0.499 Release(2010a) running on Microsoft Windows 7 operating with an Intel(R)Pentium(R) Dual Processor running at 2.10 GHZ. We solve the state equations with a guess for the controls over simulated time using forward fourth order Runge-Kutta scheme. Then those state variables are used to solve the adjoint equation equations backward in time with the final conditions(3.5), again using a fourth order Runge-Kutta method. The control u_1 and u_2

are updated and used to solve the state and then the adjoint system. The iterative process is terminated when the current states, adjoint, and control values converges sufficiently.

4.1 Optimal prevention only

With this strategy, optimal prevention only (u_1) is utilized in the control of myocardial infarction due to diabetes while the recovery control (u_2) is set to zero, with weight factors $A_1 = 50$, $B_1 = 5000$, $B_2 = 0$. For this strategy, we observed that the number of diabetic individuals susceptible is higher than when optimal prevention and recovery are absent, where the number of diabetic patients susceptible to myocardial infarction tend to zero asymptotically as seen in Figure 1. For the number of diabetic patients with myocardial infarction, the population decreases and lesser than the number of diabetic individuals with myocardial infarction when optimal prevention and recovery are absent, where the population asymptotically tends to zero in about two years as seen in Figure 1.

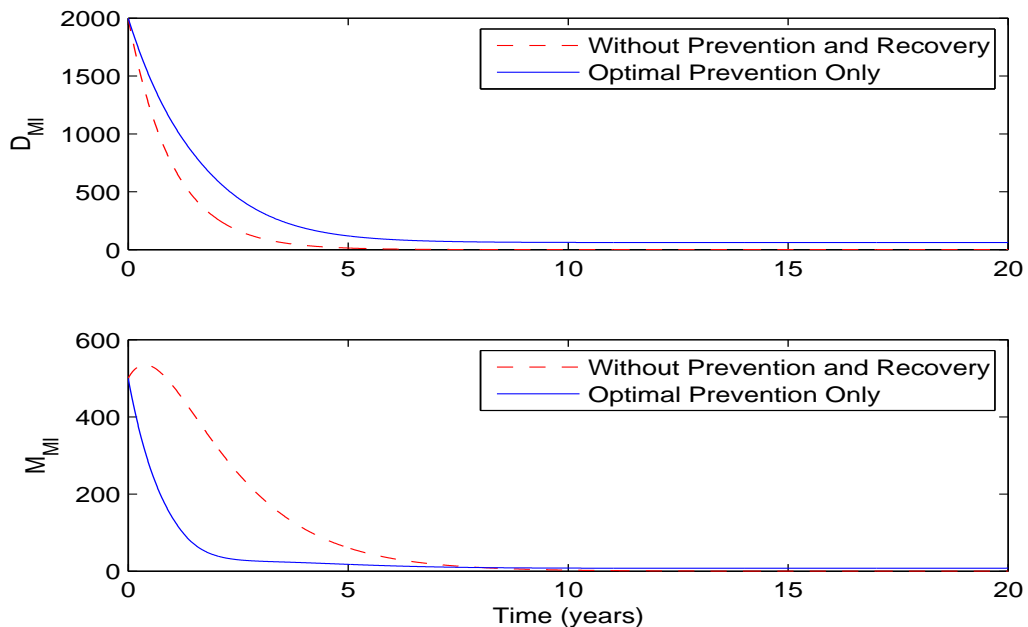


Figure 1: Simulations of the MI model (2.7)- (2.9) showing the effect of optimal prevention rate on both diabetic patients without and with myocardial infarction populations

4.2 Optimal recovery only

Here the control (u_2) on recovery is utilized while the control (u_1) on prevention is set to zero, with weight factors $A_1 = 50$, $B_1 = 0$, $B_2 = 500$. For this strategy, we observed in Figure 2 that the presence of control on recovery speeds up the rate at which the total number of diabetic individuals with myocardial infarction tends to zero compares with when optimal prevention and recovery are absent. In the case recovered population, the total number of recovered diabetic individuals is higher than the total number of recovered diabetic individuals when optimal prevention and recovery are absent, as seen in Figure 2.

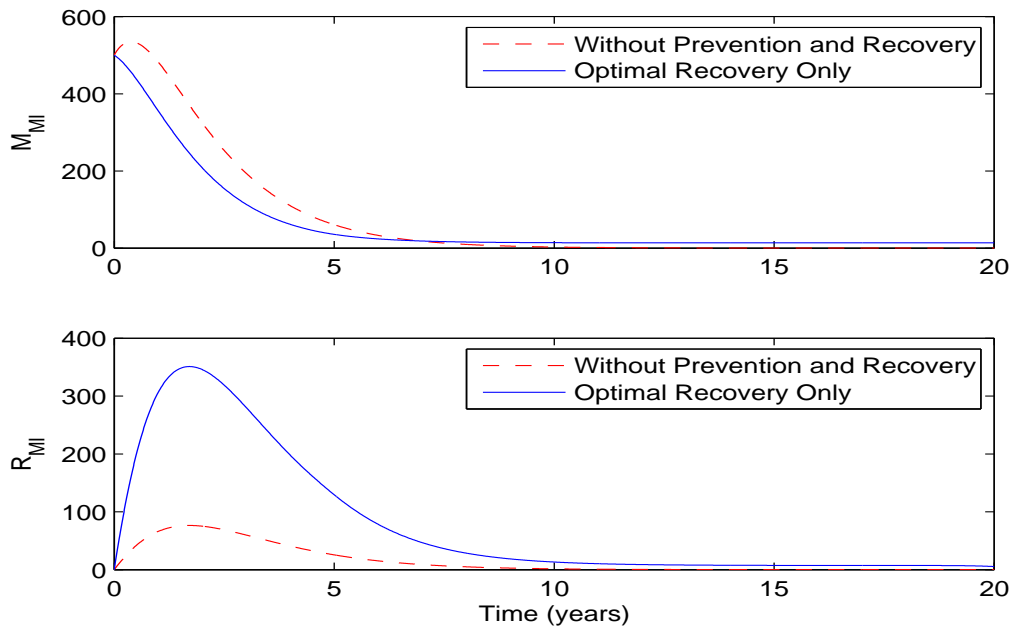


Figure 2: Simulations of the MI model (2.7)- (2.9) showing the effect of optimal recovery rate on both myocardial infarction and recovery populations

4.3 Optimal prevention and recovery

With this strategy, the controls on prevention (u_1) and recovery (u_2) are utilized with weight factors $A_1 = 50$, $B_1 = 5000$, $B_2 = 500$. For this strategy we observed in Figure 3, that the total number of diabetic individuals is lesser than the diabetic population in the absence of optimal prevention and recovery. In Figure 4, we observed that the diabetic individual with myocardial infarction decreases and approaches zero faster than in the absence of optimal prevention and recovery. The recovered population peaked in about two years in the presence of optimal prevention and recovery with a higher number in comparison to the situation when optimal prevention and recovery are absent as shown in 5. The control strategy for prevention and recovery are depicted in Figure 6 and Figure 7.

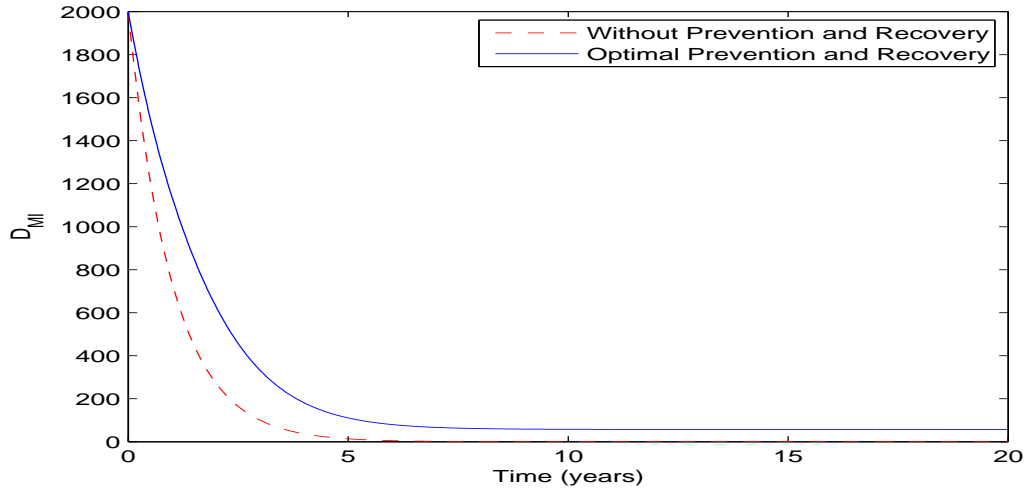


Figure 3: Simulations of the MI model (2.7)- (2.9) showing the effect of optimal prevention and recovery rates on diabetic population without myocardial infarction

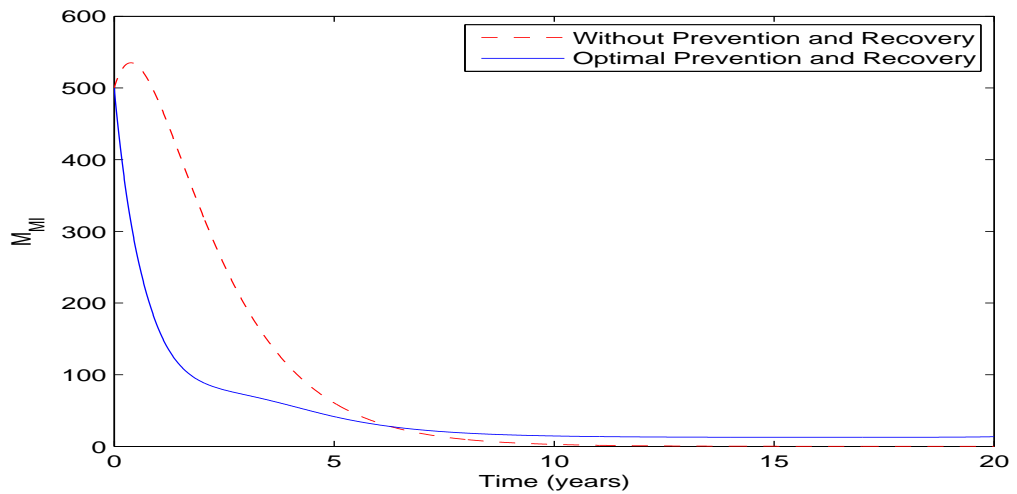


Figure 4: Simulations of the MI model (2.7)- (2.9) showing the effect of optimal prevention and recovery rates on myocardial infarction population

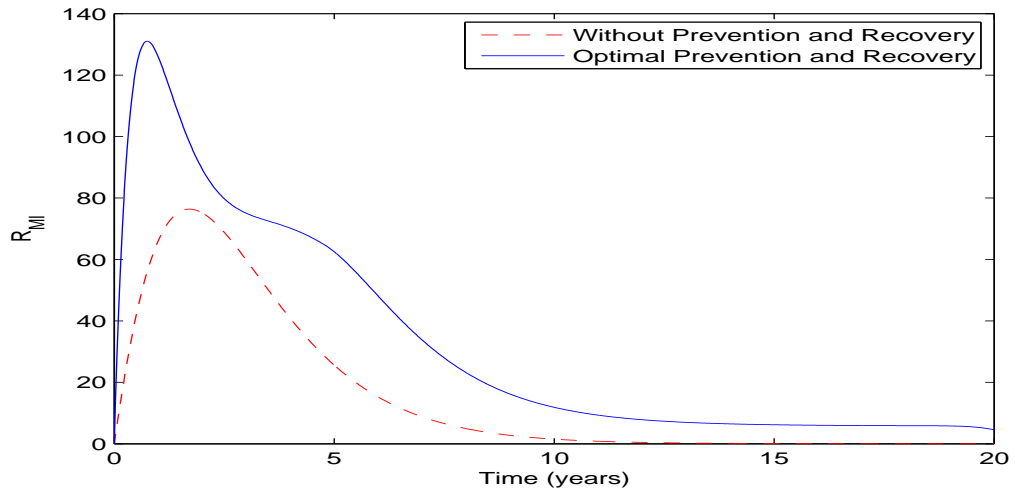


Figure 5: Simulations of the MI model (2.7)- (2.9) showing the effect of optimal prevention and recovery rates on recovery population

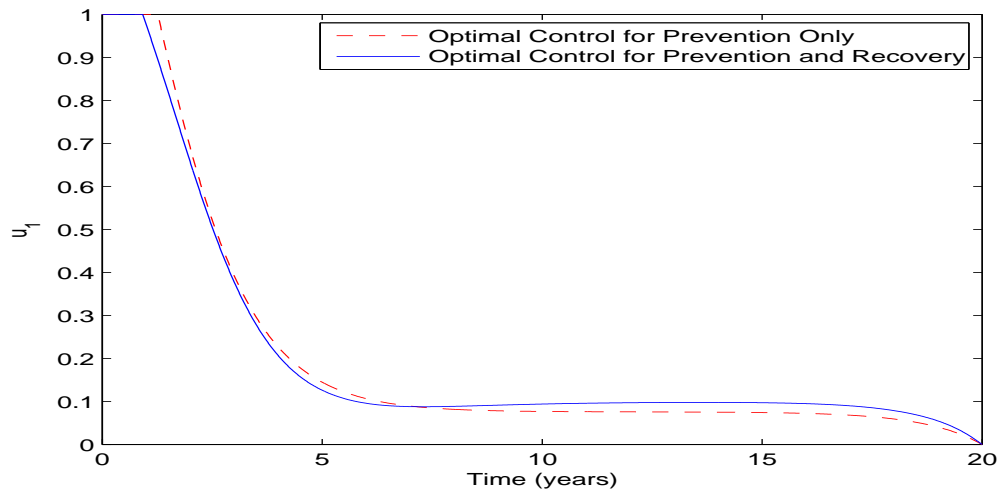


Figure 6: Optimal control for prevention

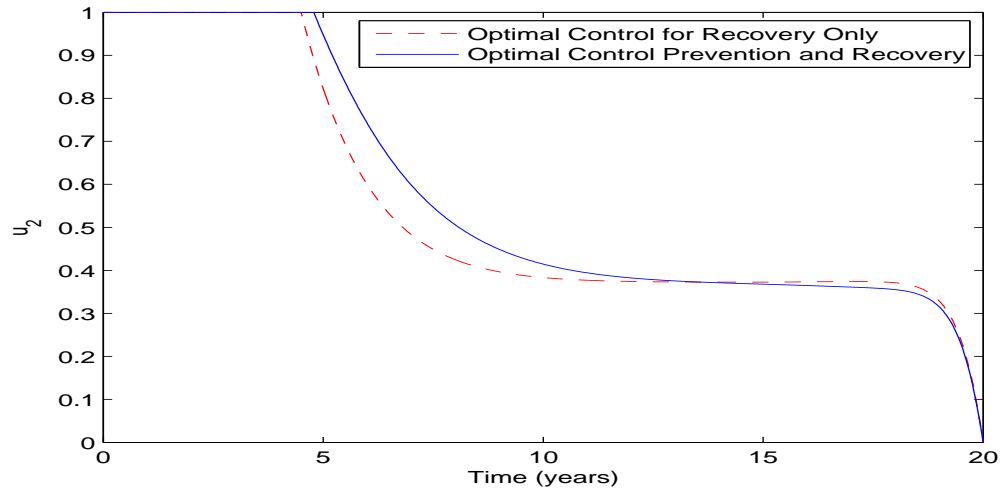


Figure 7: Optimal control for recovery

5 Conclusion

In conclusion, our optimal control results show how cost-effective combination of prevention and recovery may reduce the number of diabetic individuals with myocardial infarction. We have identified the optimal control strategies for several scenarios which yield better results in the absence of optimal prevention and recovery. Thus, control programs that follow these strategies can effectively reduce the number of diabetic individuals with myocardial infarction.

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References

- [1] Fauci, A. S. and Longo's, D. L.,(2008). Principles of Internal Medicine.(17th edition). The McGraw-Hill Companies.
- [2] McCarthy, D. and Zimmet, P.,(1994). Diabetes 1994 to 2010: global estimates and projections.Melbourne: International Diabetes Institute.
- [3] Guyton, A. and Hall, J.,(2006). Medical physiology.(11th edition).Elsevier Saunders.
- [4] Stout R. W.,(1981). Blood glucose and atherosclerosis. Arteriosclerosis vol(1):227-234.

- [5] Cowie C. C. and Eberhardt M. S.,(1996). Diabetes 1996: Vital Statistics. Alexandria, V A: American Diabetes Association, 1996.
- [6] Alajbegovic, S., Metelko, S., Alajbegovic, A., Mehmedika-Suljic E. and Resic H.,(2007). Prevalence and Significance of Diabetes in Patients with Acute Myocardial Infarction. *Diabetologia Croatica* **35-4**:75-82
- [7] Manson, J. E., Tosteson P. H., Ridker P. M., Satterfield, S., Hebert, P. H., O'Connor G. T., D.Sc., Buring J. E., and Charles H. Hennekens, C. H.,(1992). The Primary Prevention of Myocardial Infarction. *New Engl J Med* 1992; vol(**326**):1406-1416.
- [8] Duchateau, F., Devaud, M. L., Burnod, A., Mantz, J., and Ricard-Hibon, A.,(2007). A Quality Control Programme for Acute Myocardial Infarction Management in Out-of-Hospital Critical Care Medicine. *Emerg Med J.* 2007; 24(**7**): 487488.
- [9] Khajehnasiri, A. A., Khajehnasiri, N. and Shahmorad, S.,(2011). A Mathematical Model for Recovery of Myocardial Infarction Due Diabetes. *Advanced Modeling and Optimization*, vol(**13**),1:97-105.
- [10] Adekunle A.I, Aderinto Y. O. and Augusto F. B(2009).: Application of Optimal Control to The Epidemiology of Tuberculosis Transmission. *Advances in Mathematics, Proceeding of the international Conference in memory of Late Prof. C. O. A. Sowunmi*: pg 199-217.
- [11] Jung, E., Lenhart, S. and Feng, Z.,(2002). Optimal Control of Treatments in a Two-Strain Tuberculosis Model. *Discre. and Cont. Dyna. Sys.-Series B*, Vol(**2**), Number(**4**):473-482.
- [12] Pontryagin, L. S., Boltyanskii, V. G., Gamkrelidze, R. V. and Mishchenko E. F.,(1962). *The Mathematical Theory of Optimal Processes*. Wiley, New York.
- [13] Fleming, W. H. and Rishel, R. W.,(1975). *Deterministic and Stochastic Optimal Control*. Springer verlag, New York