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OPTIMAL CONTROL MODEL FOR MALE CIRCUMCISION IN HIV/AIDS PREVENTIONS

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ABSTRACT

This work presents the mathematical model of the transmission dynamics of HIV/AIDS infection with the circumcision of the susceptible and infected population. It describes the interaction between the susceptible, the infected and removed population which results in a system of ordinary differential equation The control $u_1(t)$ $u_2(t)$, $u_3(t)$ representing the efficiency of circumcised/prevention devices, efficiency of the vaccine therapy in preventing HIV infection, the efficiency of drug in inhibiting the virus strain and effort on infected human that are circumcised and those that are not circumcised to increase the number of removed individuals respectively, were introduced, resulting in a system of differential equation with optimal control The control efforts for the reduction of transmission dynamics of the infection were established using Pontryagin's Maximum Principle and optimality condition.

1. Introduction

Basically, male circumcision is the surgical removal of all or parts of the foreskin of the male reproductive organ. It can be practiced as part of a religious inclination, medical procedure or traditional /cultural ritual performed as an initiation into manhood.

Since 1980s over thirty (30) observational studies suggest a protective effect of male circumcision on HIV acquisition in heterosexual men [1]. The primary purpose of optimal control in mathematical modelling of HIV transmission is to impose a control on the various levels of circumcision administered to the different set of individuals in the population. It is also meant to project population level outcome from individual level inputs [1].

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There are many possible outcomes that can be examined with a model, for example the incidence of infection, the prevalence of infection of the. The most basic outcome, however is the likelihood of the epidemic occurring. That is, whether there is sufficient transmission potential for a chain of epidemic to be sustained.

For complex epidemic like HIV/AIDS there is no established medical cure, it is discovered that HIV/AIDS may be eradicated provided that the net transmission rate of the infected individual is sufficiently reduced [1,4,5,6,11,16].

Male circumcision has recently been shown to reduce annual susceptibility of infection with HIV by approximately 60% [Joint United Nations Programme on HIV/AIDS (2007), [2,7,8].

According to [**3,4,5.6.7,8**], over 11 million voluntary medical male circumcisions (VMMC) have been performed of the projected 20.3 million needed to reach 80% adult male circumcision prevalence in priority sub-Saharan African countries. Striking numbers of adolescent males, outside the 15-49-year-old age target, have been accessing VMMC services. They indicate that mathematical modeling can provide further insights on how to efficiently reach the male circumcision coverage levels needed to create and sustain further reductions in HIV incidence to make AIDS no longer a public health threat by 2030. They also considered the ease of implementation and cultural acceptability that decision makers may also value the estimates that mathematical models can generate the impact, cost-effectiveness, and magnitude of impact resulting from different policy choices. This supplement presents the results of mathematical modeling using the Decision Makers' Program Planning Tool Version 2.0 (DMPPT 2.0), the Actuarial Society of South Africa (ASSA2008) model, and the age structured mathematical (ASM) model. These models are helping countries examine the potential effects on program impact and cost-effectiveness of prioritizing specific subpopulation. The modeling also examines long-term sustainability strategies, such as adolescent and/or early infant male circumcision, to preserve VMMC coverage gains achieved during rapid scale-up. The 2016–2021 UNAIDS strategy target for VMMC is an additional 27 million VMMC in high HIV-prevalence settings by 2020, as part of access to integrated sexual and reproductive health services for men. To achieve further scale-up, a combination of evidence, analysis, and impact estimates can usefully guide strategic planning and funding of VMMC services and related demand-creation strategies in priority countries.

Public health challenges have been mitigated by mathematicians and epidemiologist through the use Mathematical models in studying, understanding, describing and analysing the dynamics of epidemic outbreak with the aim of preferring solutions to real life problems [7, 8,19,20,21,22,23,24,25,26,27,28,29,30]

Male circumcision has been proven to be effective in enhancing reduction in HIV/AIDS transmission in the population. [3,7]. Optimal control strategy is an established veritable tool for optimizing efforts in the reduction of disease transmission in epidemiology [10, 12, 13,15,21, 27] In the most recent research in this area, the researchers did not incorporate optimal control strategy in the work. .In this work, we seek to formulate and analyse the optimal control for the mathematical model of male circumcision in HIV/AIDS preventions resulting in differential equations which investigate efficiency of circumcised/prevention devices, efficiency of the vaccine therapy in preventing HIV infection, the efficiency of drug in inhibiting the virus strain and effort on infected human that are circumcised and those that are not circumcised to increase the number of removed individuals.

The motivation behind the introduction of an optimal condition in this work is to achieve the most effective balance between maximizing the health benefits and minimizing potential risks**,** costs**,** and unintended consequences.

Assumptions and Parameters

1.1 **Assumptions**

1. We assume that there is a proportionate recruitment rate of individuals into the heterosexual population.
2. There is proportionate rate of circumcision of both the susceptible and infected individuals.

1.2 **PARAMETERS**

$S_c(t)$= Number of susceptible individuals that are circumcised at time $t, t>0$

$S_{nc}(t)$= Number of susceptible individuals that are not circumcised at time $t, t>0$

$S(t)=S_c(t)+S_{nc}(t)=$ Susceptible population at time $t, t>0$

$I_c(t)$= Number of infected individuals that are circumcised at time $t, t>0$

$I_{nc}(t)$= Number of infected individuals that are not circumcised at time $t, t>0$

$I(t)=I_c(t)+I_{nc}(t)=$ infected population at time $t, t>0$

What is $R(t)$?

$N=S(t)+I(t)=S_c(t)+S_{nc}(t)+I_c(t)+I_{nc}(t)=$ total population under the

b = Recruitment rate into the population

μ = Natural death rate of the population

$V_c=¿$ Death rate of circumcised infected individuals

$V_{nc}=¿$ Death rate of uncircumcised infected individuals

$\sigma = The\, rate\, at\, which\, susceptible\, indiduals\, are\, being\, circumcised$

$\rho = The\, rate\, at\, which\, infected\, individuals\, are\, being\, circumcised\,.$

$\beta = The\ probability\ of\ transmission\, by\ individuals \in class\ I_{nc}$

$\alpha = The\ probability\ of\ transmission\, by\ individuals \in class\ I_c$

$c = Average\, number\, of\ contact \vee partners\ per\ unit\, time$

$c\beta \wedge c\alpha\, are\, net\ transmission\, of\ individuals \in class\ I_{nc} \wedge I_c$ respectively

2.0 The Model

The combination of the above assumptions and parameters result in the following model equation for male circumcision in HIV/AIDS preventions.

$$\frac{dS_c(t)}{dt} = \sigma S_{nc}(t) - B(t) S_c(t) - \mu S_c(t) \ldots\ldots 2.1$$

$$\frac{dS_{nc}(t)}{dt} = bN - B(t) S_{nc}(t) - \sigma S_{nc}(t) - \mu S_{nc}(t) \ldots\ldots 2.2$$

$$\frac{dI_c(t)}{dt} = B(t) S_c(t) - (\mu + v_c) I_c + \sigma I_{nc}(t) \ldots\ldots 2.3$$

$$\frac{dI_{nc}(t)}{dt} = B(t) S_{nc}(t) - (\mu + v_{nc}) I_{nc} - \sigma I_{nc}(t) \ldots\ldots 2.4$$

$$\frac{dR(t)}{dt} = v_c I_c + v_{nc} I_{nc} - \mu R(t) \ldots\ldots 2.5$$

Where

$$B(t) = \frac{c\beta I_{nc}(t) + c\alpha I_c(t)}{N} = incidence\ rate\ of\ infection$$

3.0 FORMULATION OF THE OPTIMAL CONTROL PROBLEM FOR MODEL OF MALE CIRCUMCISION IN HIV/AIDS PREVENTIONS

Given the initial population size $S_c(0), S_{nc}(0), , I_c(0), I_{nc}(0), R(0)$of all the five classes of model (2.1) – (2.5), the aim of this section is to find the best control strategy that would minimize the number of individuals that die as a result of the disease, at the same time minimizing the cost of the strategy.

Introducing the controls strategies $u_1(t)$ $u_2(t)$ and $u_3(t)$ representing the efficiency of circumcised/prevention devices, efficiency of the vaccine therapy in preventing HIV infection, the efficiency of drug in inhibiting the virus strain and effort on infected human that are circumcised and those that are not circumcised to increase the number of removed individuals respectively, the model (2.1) – (2.5) becomes Eq. (3.1) – (3.5)

$u_1(t)$is defined to be the prevention/isolation control, minimizing the contact among the healthy and infected individuals. $u_2(t)$, is the vaccination control, it represents the effort on the possible vaccination of all the individuals in order to reduce the further spread of HIV, thereby reducing the infection in the system. The control u_3 represents the treatment effort on the $I_c. -¿$ Number of infected individuals that are circumcised at time $t, t > 0$ and $I_{nc}(t)$= Number of infected individuals that are not circumcised at time $t, t > 0$. r_1, r_2, represent the rate of treatment of $I_c. -¿$ Number of infected individuals that are circumcised at time t, and $I_{nc}(t)$= Number of infected individuals that are not circumcised respectively.

The above illustrations and parameters leads to the following optimal control problem for male circumcision in HIV/AIDS prevention

$$\frac{dS_c(t)}{dt}=\sigma S_{nc}(t)(1-u_2)-B(t)S_c(t)(1-u_1)-\mu S_c(t)\ldots\ldots\ldots\ldots\ldots\ldots 3.1$$

$$\frac{dS_{nc}(t)}{dt}=bN-B(t)S_{nc}(t)-\sigma S_{nc}(t)(1-u_2)-\mu S_{nc}(t)\ldots\ldots\ldots\ldots\ldots 3.2$$

$$\frac{dI_c(t)}{dt}=B(t)S_c(t)(1-u_1)-(\mu+v_c)r_1 I_c(1-u_3)+\sigma I_{nc}(t)\ldots\ldots\ldots 3.3$$

$$\frac{dI_{nc}(t)}{dt}=B(t)S_{nc}(t)-(\mu+v_{nc})I_{nc}r_2(1-u_3)-\sigma I_{nc}(t)\ldots\ldots\ldots\ldots\ldots\ldots 3.4$$

$$\frac{dR(t)}{dt}=v_c I_c r_1(1-u_3)+v_{nc}I_{nc}r_2(1-u_3)-\mu R(t)\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots 3.5$$

The control functions $u_1(t)$ $u_2(t)$ and $u_3(t)$, are bounded lebesgue integrable functions.
The control $u_1(t)$ is the time dependent effort on prevention/isolation control on the circumcised, minimizing the contact among the healthy and infected individuals., practiced on the time interval $[0,t¿¿f]¿$ to reduce the number of individuals that may become fully infected.
The control $u_2(t)$ is the time dependent effort on the efficiency of the vaccine therapy on the non-circumcised individuals in preventing new HIV/AIDS, practiced on the time interval $[0,t¿¿f]¿$ to reduce the number of individuals that may become fully infected
The control $u_3(t)$ is the time dependent effort on the treatment effort on the actively infected individuals (I_c. I_{nc}), practiced on the time interval $[0,t¿¿f]¿$ to increase the number of removed individuals

The optimal control problem in this work, involves that in which the number of circumcised and non-circumcised susceptible individuals, active HIV/AIDS infections and the cost of treatment controls $u_1(t)$ $u_2(t)$, $u_3(t)$, , are minimized subject to the differential Equations $(3.1)-(3.5)$. This involves the number of individuals with circumcised and non-circumcised HIV/AIDS infection respectively as well as the cost of carrying out circumcision exercise and vaccine therapy in preventing new HIV/AIDS, the efficiency of drug in inhibiting the virus strain and effort on infected human to increase the number of removed individuals.
The objective functional is defined as

$$J=\int_0^{t_f}\{A_1 I_c+A_2 I_{nc}+\frac{A_3}{2}u_1^2+\frac{A_4}{2}u_2^2+\frac{A_5}{2}u_3^2\}\,dt\ldots\ldots\ldots\ldots\ldots\ldots(3.6)$$

Where t_f is the final time and the coefficient $A_1>0, A_2>0, A_3>0, A_4>0, A_5>0$,are the balancing cost factors.

We seek to minimize the objective functional

$$J=\int_0^{t_f}\{A_1 I_c+A_2 I_{nc}+\frac{A_3}{2}u_1^2+\frac{A_4}{2}u_2^2+\frac{A_5}{2}u_3^2\}\,dt$$

Subject to the optimal control system (3.1) – (3.5)
Hence minimizing the number of infected individuals but keeping the cost of circumcision, treatment/drugs low. That is, to find the optimal control u_1^0,u_2^0,u_3^0, such that $J(u_1^0,u_2^0,u_3^0)=Min¿$ $u_2(t), u_3(t)\,¿/u_1(t), u_2(t), u_3(t)\epsilon\,\Omega\,¿$

Where $\Omega = \{ ¿\, u_2(t), u_3(t)\ ¿/u_1(t)\, u_2(t), u_3(t)\ are\, measurable \}$
$a_i < u_1(t)\, u_2(t), u_3(t)\, ¿\, b_i, i=1,2,3\, t \epsilon [0, t_f]$ is the control set. Also $a_i . \wedge b_i\, are\, constant \in [0,1]$
We use the quadratic control functions in this problem because the controls cost of intervention is nonlinear. It means that there is
no linear relationship among the cost of intervention among infected individuals and the cost of intervention.

3.5 Characterization of an Optimal Control
We shall apply the Pontryagin's Maximum Principle [9,10,12,13,14,17,18,19], to convert the system (3.1) – (3.5) and (3.6) to a problem of minimizing a pointwise Hamiltonian functional with respect to the controls u_i . And also establish necessary conditions for the optimal control of the system.
We take $\lambda_k, \forall k = S_c, S_{nc} I_c, I_{nc}, R$ to be the adjoint variable associated with the state variable $S_c, S_{nc} I_c, I_{nc}, R$.
Theorem 3.3: Given the optimal control u_j^0 and solutions $S_c^0, S_{nc}^0, I_c^0, I_{nc}^0,, R^0$ of the control system (3.1) – (3.5) that minimizes $J \frac{(u_j^0)}{\Omega}$. Then there exist adjoint variables λ_k satisfying

$$\frac{\partial \lambda_k}{\partial t} = \frac{-\partial H}{\partial i} \ldots\ldots\ldots\ldots\ldots..(3.7)$$

With transversality conditions

$$\lambda_k(t_f) = 0, where\, k = S_c, S_{nc} I_c, I_{nc}, R \ldots .(3.8)$$

The optimality condition is given by

$$\frac{\partial H}{\partial u_j} = 0, \forall j = 1,2,3 (3.9)$$

With controls $u_1^0 = min \left\{ 1, max \left[0, \frac{B S_c^0 \{ \lambda_3^{¿} - \lambda_1^{¿} \}}{A_3} \right] \right\}$

$$u_2^0 = min \left\{ 1, max \left[0, \frac{\sigma S_{nc}^0 \{ \lambda_1^{¿} - \lambda_2^{¿} \}}{A_4} \right] \right\}$$

$$u_3^0 = min\, ¿$$

PROOF:

Since we have five state variables, $S_c, S_{nc} I_c, I_{nc}, R$, we shall have five corresponding adjoint variables $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5$. Then we obtain the Hamiltonian functional:

$$H = A_1 I_c + A_2 I_{nc} + \frac{A_3}{2} u_1^2 + \frac{A_4}{2} u_2^2 + \frac{A_5}{2} u_3^2 + \lambda_1 \{ \sigma S_{nc}(t)(1-u_2) - B(t) S_c(t)(1-u_1) - \mu S_c(t) \} + \lambda_2 \{ bN - B(t) S_{nc}(t) - \sigma S_{nc}(t$$

The system of adjoint equation is obtained by taking the appropriate partial derivative of H with respect to the respective state variables.

$$\frac{\partial \lambda_{S_c}}{\partial t} = \frac{\partial \lambda_1}{\partial t} = \frac{-\partial H}{\partial S_c} = \lambda_1 \{ B(t)(1-u_1) + \mu \} - \lambda_3 B(t)(1-u_1)$$

$$\lambda_{S_c}(t_f) = 0$$

$$\frac{\partial \lambda_{S_{nc}}}{\partial t}=\frac{\partial \lambda_2}{\partial t}=\frac{-\partial H}{\partial S_{nc}}=-\lambda_1\sigma\left(1-u_2\right)-\lambda_2\left\{-B(t)-\sigma\left(1-u_2\right)-\mu\right\}-\lambda_4 B(t)$$

$$\lambda_{S_{nc}}\left(t_f\right)=0$$

$$\frac{\partial \lambda_{I_c}}{\partial t}=\frac{-\partial H}{\partial I_c}=-A_1+\lambda_3\left(\mu+v_c\right)r_1\left(1-u_3\right)-\lambda_5 v_c r_1\left(1-u_3\right)$$

$$\lambda_{I_c}\left(t_f\right)=0$$

$$\frac{\partial \lambda_{I_{nc}}}{\partial t}=\frac{-\partial H}{\partial I_{nc}}=-A_2-\lambda_2\sigma+\lambda_4\left\{\left(\mu+v_{nc}\right)r_2\left(1-u_3\right)-\sigma\right\}-\lambda_5 v_{nc} r_2\left(1-u_3\right)$$

$$\lambda_{I_{nc}}\left(t_f\right)=0$$

$$\frac{\partial \lambda_R}{\partial t}=\frac{-\partial H}{\partial R}=\lambda_5\mu$$

$$\lambda_{I_R}\left(t_f\right)=0$$

The optimal control u_1^0, u_2^0, u_3^0 can be solved from optimality conditions

$$\frac{\partial H}{\partial u_1}=A_3 u_1+\lambda_1 B(t)S_c(t)-\lambda_3 B(t)S_c(t)=0$$

$A_3 u_1+\lambda_1 B(t)S_c(t)-\lambda_3 B(t)S_c(t)=0$

$$u_1^0=\frac{BS_c^0\left(\lambda_3^{¿}-\lambda_1^{¿}\right)}{A_3}$$

$$\frac{\partial H}{\partial u_2}=A_4 u_2-\lambda_1\sigma S_{nc}(t)+\lambda_2\sigma S_{nc}(t)=0$$

$$A_4 u_2-\lambda_1\sigma S_{nc}(t)+\lambda_2\sigma S_{nc}(t)=0$$

$$u_2^0=\frac{\sigma S_{nc}^0\left(\lambda_1^{¿}-\lambda_2^{¿}\right)}{A_4}$$

$$\frac{\partial H}{\partial u_3}=A_5 u_3+\lambda_3\left(\mu+v_c\right)r_1 I_c+\lambda_4\left(\mu+v_{nc}\right)I_{nc}r_2-\lambda_5 v_c I_c r_1-\lambda_5 v_{nc} I_{nc} r_2=0$$

$$u_3^0=\frac{\lambda_5^{¿}(v¿¿nc\, I_{nc}^0 r_2+v_c I_c^0 r_1)-\lambda_4^{¿}\left(\mu+v_{nc}\right)I_{nc}^0 r_2-\lambda_3^{¿}\left(\mu+v_c\right)r_1 I_c}{A_5}¿$$

SUMMARY AND CONCLUSION

In this study, we present the mathematical model of the transmission dynamics of HIV/AIDS infection with the circumcision of the susceptible and infected population. It describes the interaction between the susceptible, the infected and removed population which results in a system of ordinary differential equation (2.1) -(2.5). The control $u_1(t)\ u_2(t),\ u_3(t)$ representing the efficiency of circumcised/prevention devices, efficiency of the vaccine therapy in preventing HIV infection, the efficiency of drug in inhibiting the virus strain and effort on infected human that are circumcised and those that are not circumcised to increase the number of removed individuals respectively, were introduced, resulting in a system of differential equation with optimal control (3.1)-(3.5). The system (3.1) -(3.5) were analysed using Pontryagin's Maximum Principle and optimality condition. The controls

$$u_1^0 = \frac{B S_c^0 \left(\lambda_3^{¿} - \lambda_1^{¿} \right)}{A_3}$$

$$u_2^0 = \frac{\sigma S_{nc}^0 \left(\lambda_1^{¿} - \lambda_2^{¿} \right)}{A_4}$$

$$u_3^0 = \frac{\lambda_5^{¿} \left(v ¿¿ nc\, I_{nc}^0 r_2 + v_c I_c^0 r_1 \right) - \lambda_4^{¿} \left(\mu + v_{nc} \right) I_{nc}^0 r_2 - \lambda_3^{¿} \left(\mu + v_c \right) r_1 I_c}{A_5} ¿$$

Are aim at reducing the rate of transmission

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