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A Mathematical Model of Cervical Cancer in Kenya

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Abstract: ***Background: In this paper dynamic models for cervical cancer among women with diagnosed and undiagnosed cervical cancer have been constructed. Methods: Differential equations for the population of women in each stage of diagnosed and undiagnosed cervical cancer were developed. The year 2010 was used as the base year. The equations were run through Matlab™ and results are presented in graphs. Results and Discussion: The growth patterns for both diagnosed and undiagnosed status in the population were identical. However, the only difference between the two has been observed as the initial values that are estimated from the WHO/ICO report taking 2010 as the base year for the respective stages. This was with assumption of no change in detection process.***

Keywords: Cervical cancer, mathematical modeling, Kenya, stages

1. Background and Literature Review

Models are representations or abstractions of actual objects, processes, situations or any features a researcher wishes to describe or whose behavioral pattern is being studied and analyzed. Mathematical models describe the undertaken aspect in a precise way and assist in arriving at reasonably accurate estimates, by using various branches and procedures of mathematics. Mathematical models help in indicating what information should be collected and in what amount. If the boundary of analysis is selected appropriately, it is possible to deal with the undertaken problem in its totality and allow consideration of all major variables of the problem simultaneously.

In this paper mathematical models for cervical cancer among women for diagnosed and undiagnosed stages are developed and the impacts of vaccinations as well as screening intervention strategies are analyzed. Cervical cancer is estimated to account for 15% of all female cancers and cause approximately 46,000 deaths each year in women aged 15-49 years in developing countries (WHO/ICO 2010). It is the second most frequent cancer after breast cancer in Kenya among women between age of 15 to 44 years(WHO/ICO 2010). For the purposes of this model 2010 was considered the base year. According to United Nations Development program (UNDP) the projection of female population in Kenya regardless of age as at year 2010 was 20,492,000, while those females aged 10 to over 65years comprised 14,260,000. The World Health Organization(WHO) report documented the incidences of Human papillomavirus(HPV) in intervals of 10 years from age of less than 14 years, 15 to 44 years, 45 to 54 years, 55 to 64 years and over 65 years(WHO/ICO 2010). Baseline data was derived from the WHO/ICO report (WHO/ICO 2010).

Different preventive and intervention approaches have been proposed in the management of cervical cancer. These include pre-exposure /primary vaccination of pre-pubertal girls and secondary /catch up vaccination of women aged between 10 and 45 years. Currently two main vaccines are available. Gardasil is only given to females' aged 9 to 26(Elbasha, Dasbach, and Insinga 2007)(Lee and Tameru 2012). A complete cycle of HPV vaccine is given in three equal doses over a period of six months. The second dose is given 1 to 2 months after the first dose while the last dose is given at six months after the first dose. Women who are pregnant should not get the HPV vaccine until after the baby is born. Cervarix is recommended for 10 to 45 year olds (Baussano et al. 2013)(Situations 2010) (Markowitz et al. 2007).

Different screening methods have also been employed. The methods have differing sensitivity and specificity levels. These methods include Visual Inspection with Acetic Acid (VIA), Visual Inspection with Lugol's Iodine (VILLI), DNA Testing and Cytology (Duraisamy et al. 2011). Clinical management of cervical cancer includes surgical intervention, chemotherapy, radiotherapy or any combination of these methods have been employed(Legge et al. 2010; Mucheusi 2012).These management approaches have different impacts on the number of patients undergoing progression and regression at various stages of cervical cancer.

Currently, the Kenyan Government has a mix of policies, comprising advocating to abstinence, being faithful, use of visual inspection with acetic acid (VIA) and visual inspection with Lugol iodine (VILLI). This model analyses the impact of vaccination and screening interventions in Kenya. The models assume vaccination of pre-adolescent girls at the age of after 9 years and before turning 10 years. This period for vaccination has been chosen since the conversion of dormant columnar epithelium of endo-cervical canal into squamous epithelium has not yet occurred, hence the cells are still not susceptible to Human Papillomavirus (HPV) infection (Martens et al. 2009)(Di Bonito and Bergeron 2012). The efficacy of the vaccine is assumed to be lifelong and the girls who received primary vaccination

permanently exit the model as the model follows the females with HPV infection.

2. Problem Statement

Unless the impact of different interventions in cervical cancer is mapped, it is unreasonable to expect the cervical cancer managers to develop sound policies. In this paper mathematical models for cervical cancer among women for diagnosed and undiagnosed stages are developed and the impacts of vaccinations, treatment as well as screening intervention strategies are analyzed. If the boundary of analysis is selected appropriately, it is possible to deal with the undertaken problem in its totality and allow consideration of all major variables of the problem simultaneously.

3. Methods

The overall approach utilized in this paper is dynamical modeling. In this model differential equations along with boundary conditions were formulated. To describe the Mathematical modeling has been done in line with HIV/AIDS infection model, using differential equations by Simwa and Pokhariyal(Simwa and Pokhariyal 2003). Simwa and Pokaryal used dynamical, two systems of ordinary differential equations to model the HIV/AIDS epidemic in Sub-Saharan Africa, and generated curves which shown the stage specific prevalence rates. The simulated results were consistent with previously published epidemiological reports in terms of non decreasing functions of time. Lee &Tameru(Lee and Tameru 2012) used a compartmental mathematical model of HPV and its impact in cervical cancer among African American women. The model included the choices individuals make once they become infected; treatment versus no treatment. Lee and Tameru(Lee and Tameru 2012)concluded that 'Mathematical models, from individual and population perspectives, would help decision makers to evaluate different prevention and mitigation scenarios of HPV' pg 268.

Adopting similar concepts, we developed compartmental models of the population of females in different stages of cervical cancer in Kenya. While the equations of Lee &Tameru(2012) provided the general functional relationship between the change in X(the susceptible, recovered and other classes of non-infected individuals) and Y and Z with time, our differential equations represent the rate of change in the number of girls and women at the different stages and diagnostic status of cervical cancer. The impact of primary vaccination, secondary vaccination, screening and treatments were incorporated and their impacts on the trends of cervical cancer in Kenya were explored using several scenarios. The model assumes that:

- *All the females seeking vaccination will complete the full dose of vaccine.*
- *The 38.8% of all the never vaccinated females will acquire HPV infection based on the prevalence of HPV in Kenya.*

number of girls and women in various stages of HPV infection (Table 1), corresponding differential equations showing the rates of change in the number of girls and women in respective stages with relevant parameter estimation were formulated.

Table 1: Distribution of HPV Infected Women

Stage of Diagnosed Cervical Cancer	*Percentage*	*Number of Women*	*Stage of Undiagnosed Cervical Cancer*	*Percentage*	*Number of Women*
m_0	5	1442	w_0	5	43621
m_1	5	1442	w_1	5	43621
m_2	10	2884	w_2	10	87242
m_3	40	11536	w_3	40	348967
m_4	40	11536	w_4	40	348967
Total	100	M= 28840		100	W= 872418

- *The females who missed both primary and secondary vaccination are eligible for screening against HPV and some women later may also miss this vital intervention. However, screened women detected will be subjected to appropriate treatment.*
- *The HPV infection among the unscreened women will progress naturally except those subjected to treatment.*
- *The vaccinated women may die from other causes other than cervical cancer as well as due to age, hence exit the model.*
- *This being a deterministic model using differential equations, there was no need of accounting for confidence intervals.*

The girls and women were stratified according to the following categories.

$$k = number\ of\ infant\ girls\ (aged\ less\ than\ 1\ year)$$

g = infant mortality rate in Kenya
i = immunized girls (aged 1-9 years) due to physiologically derived factors
v = girls who received primary vaccination at age completing 9 years
s = susceptible (girls or women age > 9 years) who missed primary
h = number of infected women in the population
f = the number of girls and women who missed the primary vaccination and are given secondary (catch up) vaccination.
r = the women aged 15 years and over who are eligible for screening
M
$= the\ number\ of\ screened\ girls\ and\ women\ who\ have\ been\ con$
W=the number of unscreened women who also have HPV infection.

This number*(M)* is further stratified as:

- Diagnosed dysplasia, denoted by m_0
- Diagnosed stage 1, denoted by m_1
- Diagnosed stage 2, denoted bym_2

- Diagnosed stage 3, denoted by m_3
- Diagnosed stage 4, denoted by m_4

Such that $M = m_0 + m_1 + m_2 + m_3 + m_4$ *(Eq 1)*

The women who missed primary and secondary vaccination as well as screening are denoted by *W*. It is assumed that this population of women may be infected with HPV and undergoes the similar stages of cervical cancer though undiagnosed. This population is further stratified as:

- undiagnosed dysplasia, denoted by w_0
- undiagnosed stage 1, denoted by w_1
- undiagnosed stage 2, denoted by w_2
- undiagnosed stage 3, denoted by w_3
- undiagnosed stage 4, denoted by w_4

Such that $W = w_0 + w_1 + w_2 + w_3 + w_4$ *(Eq 2)*

It is assumed that *80%* of the clients who may have detected cancer at the time of infection have natural clearance of HPV infections.

Let q = number of women who had HPV infection but clear naturally.

The women exit from the model through three main ways;

- through permanent immunity (z_1) via primary and secondary vaccination, such that $z_1 = v + f$ *(Eq 3)*
- Death as a result of undiagnosed cancer(z_2)
- Death from diagnosed cancer (z_3)
- Thus, the total number of women exiting the model at any given time $= v + f + z_2 + z_3 = z_1 + z_2 + z_3$ *(Eq4)*

Representation of females at various stages and the rate of change in these stages were done using differential equations.

The boundary conditions for respective stages were derived from data of WHO country report for Kenya(WHO/ICO 2010)

(i) $\frac{dk}{dt} = 0$ *when* $0 \le t \le t_s$ and $k_0 >$ 600,000 and $o \le t \le t_s$ and $k_0 > 600{,}000$ and $\frac{dk(t)}{dt} = \alpha_1 (k - g)$ *(Eq 5)*

(ii) $\frac{di}{dt} = 0$ *when* $l \le t \le 9$ and $i(t_0) = 5{,}632{,}400$ *(Eq 6)*

(iii) $\frac{dv}{dt} = \alpha_2 z(i - v), i \le t \le 9$ *and* $v(t0) =$ 16,896 *(Eq 7)*

(iv) $dh/dt = \alpha_3 (s - h)$ *(Eq 8)*

(v) $\frac{df(t)}{dt} = \alpha_4 (s - f)$, *when* $t > 10$ *and* $t <$ t_l; $f(t_0) =$ 34,947 *(Eq 9)*

(vi) $dq(t)/dt = o$, *when* $t < 15$ *and* $t > 80$; $q(t_0) =$ 11,614,157 *(Eq 10)*

(vii) $dr(t)/dt = \alpha_5(q - h)$, *when* $t < 15$ *and* $t >$ 80; $r(t_0) =$ 371653 *(Eq 11)*

(viii) $dM(t)dt = \alpha_6(r - M)$ *when* $15 < t < 65, M(t_0) =$ 144,201. *(Eq 12)*

By using the various stages of M, we get the equations for each stage, which can then be expressed graphically to show the corresponding pattern. The pattern of change from one stage to another is similar in both the diagnosed and undiagnosed situations. However, the number of cases at respective stages at the base year of 2010 is different.

4. Results

a) Diagnosed Dysplasia

Dysplasia stage is characterized by HPV presence however there is no conversion of epithelial cells to cancerous stage. Let the number of women in the dysplasia stage be denoted by $m_0(t_0)$ which is assumed to be at constant up to time t_s. then we have $dm_0(t)/dt = 0$, when $0 \le t \le t_s$ and $m_0(t_0) \le 1442 \le m_0(t)$ *(Eq 13)*

The total number of women with diagnosed dysplasia is proportional to the number of women susceptible to HPV and who underwent screening and the number of women who with medical intervention regress from stage 1 to dysplasia minus the number of women who progress from dysplasia to Stage 1. Therefore, the rate of change in the population of women with diagnosed dysplasia can be expressed as;

$\frac{dm_0(t)}{dt} \propto (r)(m_1)$. *(Eq 14)*

Changing the proportionality this gives

$\frac{dm_0(t)}{dt} = \alpha_7 r + \beta_1 m_1 - \alpha_8 m_1$ *(Eq 15)*

where $\alpha_7 = 0.2$ which is the progression factor of HPV from normal cells to m_0. This constant depends on; Virulence of HPV, General health status of the cervix and healthy living behavior of the client. $\alpha_8 = 5\%$ depicts the progression factor from m_0 to m_1; $\beta_1 = 0.8$ represents regression factor (due to treatment intervention/natural clearance)

$r = 1$ (Constant of proportionality r is taken as 1 for simplicity)

$d\,m_0(t)\,/dt = 0.2 + 0.8m_1 - m_1 = 0.2 - 0.2m_1 = m_1 =$ 1442 *(Eq 16)*

$m_0 = (\alpha_7 r + \beta_1 m_1 - \alpha_8 m_1)t + k$ *(Eq17)*

The output is as illustrated in Figure 1.

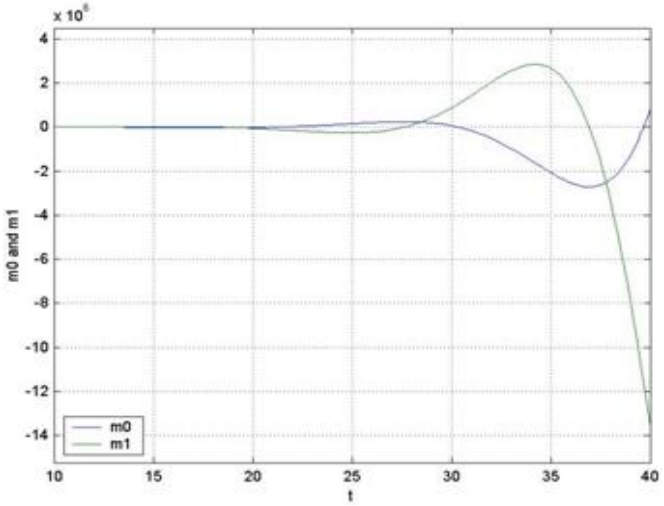

Figure 1: Progression from Diagnosed Dysplasia (m_0)to Diagnosed Stage (m_1)

There is a gradual increase in m_0 until t_{29} after which m_o decreases up to t_{38} The period t_{38} to t_{40} is characterized by an increase in m_0. At the same time m_1 is marked by gradual increase up to t_{34} and thereafter m_1 decreases sharply up to

t_{40}. This sharp decline in the rate of change in m_1 may be explained by the regression of m_1 tom_0 . Hence as the rate of change in m_1 declines, therate of change of $m_0$increases slightly.

b) Diagnosed Stage 1

The initial number of women at Diagnosed stage 1 be denoted by$m_1(t_0)$ which is assumed to be at constant up to timet_s. Let $m_1(t)$ be the number of women at stage 1 at any time$t>t_s$. The rate of change and the boundary condition are therefore;

$dm_l(t)/dt = 0$, when$0 \le t \le t_s$, $m_1(t_0)$ = 1442 and $t > t_l$

The total number of women with stage 1 among the diagnosed women is proportional to the number of women with dysplasia and the number of women who regress from stage 2 to stage 1.

Thus, the rate of change in the population of women at diagnosed stage one is expressed as,

$\frac{dm_1(t)}{dt} = \alpha_9 m_0 + \beta_2 m_2 - \alpha_{10} m_2$. *(Eq 18)*

Where;

α_9 =1, is the progression factor from dysplasia to stage1,

β_2 =0.5, is the regression factor from stage 2 to stage 1,

α_{10} =2, is progression factor from stage 1 to stage 2.

Time of progress from dysplasia to stage 1 is approximately 15 years and the time taken to regress from stage 1 to dysplasia is 1.4 years (Schlecht et al. 2003).

$\frac{dm_1(t)}{dt} = m_0 + 0.5m_2 - 2m_2 = m_0 + 1.5m_2$ *(Eq 19)*

The results are illustrated in Figure 2.

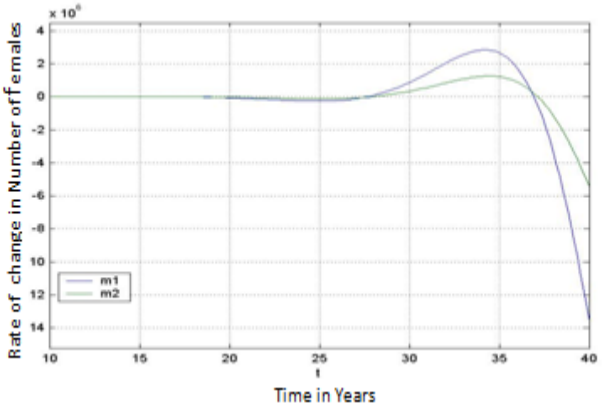

Fig 2. **Progression from Diagnosed Stage 1(m_1) to Diagnosed Stage 2(m_2)**

The progression from$m_1$to m_2 is characterized by a relatively slight increase between$t_{10}$and t_{20}. However aftert_{20} there is slight increase in both m_1 and $m_2$uptot_{30} after which there is a higher increase inm_1 uptot_{35}. This is explained by the regression of a number of cases from$m_2$to m_1.

c) Diagnosed Stage 2

Let the initial number of women at diagnosed stage 2 be denoted by $m_2(t_0)$which is assumed to be at constant up to timet_s. Let $m_2(t)$ be the proportion of women at stage 2 at any time $t > t_s$.

Thus we have $\frac{dm_2(t)}{dt} = 0$when $0 \le t \le t_s$and$m_2(t_0) \le 2884 \le m_2(t)$

Thus, the rate of change of the population of women with diagnosed stage 2 is expressed as;

$d\frac{m_2(t)}{dt} = dx\,\alpha_{11} m_1 - \alpha_{12} m_2 - \beta_3 m_2$. *(Eq 20)*

Where

α_{11}=2, is a constant dependent on progression factor from stage 1 to stage 2

α_{12} =4, is a constant that depends on the progression factor from stage 2 to stage 3

β_3 =0.5, is constant representing regression from stage 2 back to stage 1.

$m_1$is obtained from previous equation

$dm_2(t)/dt = 2m_1 - 4m_2 - 0.5m_2 = 2m_1 - 4.5m_2$ *(Eq 21)*

Time of progress from stage 1 to stage 2 is estimated to be 5.6 years and the time taken to regress from stage 2 to stage 1 is 1 year(Schlecht et al. 2003).

Even though the modelers appreciate possibility of death among the women diagnosed with dysplasia, stage 1 and stage 2 of cervical cancer, the death rates were assumed negligible for this study hence were not included in the model. The graphic behavior is as illustrated in Figure 3,

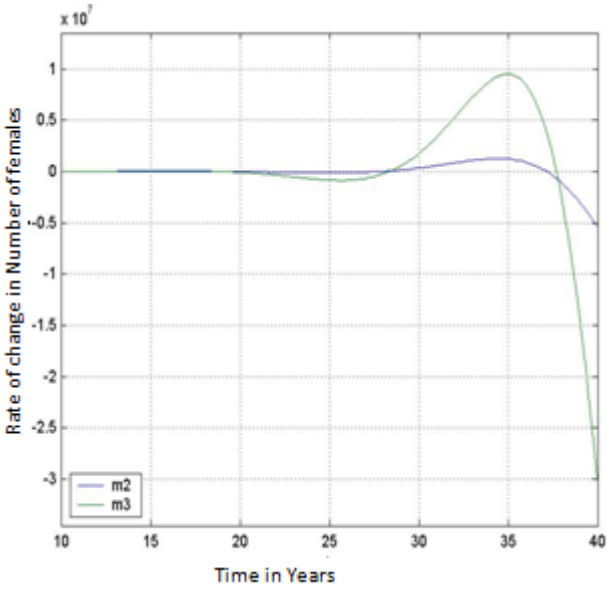

Figure 3: Progression from Diagnosed Stage 2(m_2) to Diagnosed Stage 3(m_3)

which shows that m_2 and m_3 are both constant up tot_{22} . The m_3 shows slight decrease betweent_{22} to t_{28} where as m_3 still remains constant. . It is noted that the rate of progression of m_3 declines drastically fromt_{35} . Aftert_{28}, there is a slight increase in m_2, but $m_3$increases sharply up tot_{35} . The progression rate of $m_3$declines sharply as compared to $m_2$after t_{35} . This can be attributed to the deaths at m_3

d) Diagnosed Stage 3

Let the initial number of women at diagnosed stage 3, be denoted by $m_3(t_0)$ which is assumed to be at constant up to timet_s. Let $m_3(t)$ be the number of women at stage 3 at any time t is $>t_s$and $m_3(t_0)$=11536.

Therefore the rate of change among the population of women with diagnosed stage 3 is;

$\frac{dm_3(t)}{dt} = \alpha_{13} m_2 - \alpha_{14} m_4 - \beta_4 m_3$ *(Eq 22)*

α_{13}=4, is a constant dependent on progression factor from stage 2 to stage 3

α_{14}=1, is a constant that depends on the progression factor from stage 3 to stage 4

β_1 =1, is constant representing deaths at stage 3

$dm_3(t)/dt = 4m_2 - m_4 - m_3$ *(Eq 23)*

Time of progress from stage 2 to stage 3 is estimated at 6.1 years (Schlecht et al. 2003). The model also assumes there is no regression from stage 3 to stage 2. Figure 4 further elaborates the trends of progression from stage 3 to stage 4.

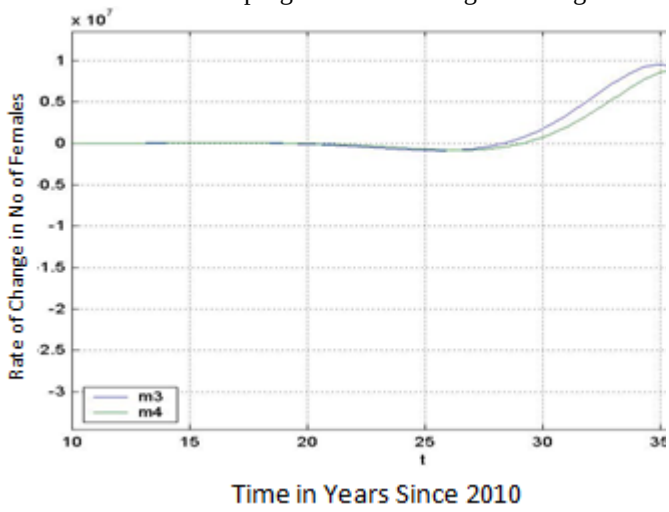

Figure 4: Diagnosed Stage 3(m_3) and Diagnosed Stage 4(m_4).

e) Diagnosed Stage 4

Let the initial number of women at diagnosed stage 4 be denoted by $m_4\ (t_0)$ which is assumed to be at constant up to time t_s.Let $m_4\ (t)$ be the proportion of women at stage 4 at any time *when* $t > t_s$and $m_4\ (t_0)$= 11536

The rate of change in the total number of women with stage 4 among the diagnosed women is

$dm_4(t)/dt = \alpha_{15} m_3 - \beta_5 m_4$. *(Eq 24)*

α_{15}=1, is a constant dependent on progression factor from stage 3 to stage 4

β_5=1, is constant representing deaths at stage 3

$dm_4(t)/dt = m_3 - m_4$ *(Eq 25)*

Time taken for cancer to progress from stage 3 to stage 4 is 1 year(Schlecht et al. 2003)

Figure 4 shows that the progression of both m_3 and $m_4$is constant up to time t_{20} and shows a slight decrease upto t_{27}. There after $m_3$has relatively higher increase up tot_{35}as compared to m_4. This is followed by a sharp decrease in m_3 as compared to $m_4$up to t_{40}. This can be attributed to the fact that deaths at stage three, would leave relatively smaller number to die at stage 4.

The coefficients of the model are estimated as the basis of the HPV infected women data for diagnosed and undiagnosed patients. Based on the proportionalities in Table 1, the trends of the diagnosed and undiagnosed patients are expected to be similar.

Unscreened and Undiagnosed Cervical Cancer Cases.

In this section the fate of the women who do not undergo screening and the stages they undergo in relation to cervical cancer are discussed. The women who missed screening and have undiagnosed HPV infections develop cervical cancer and advance to different stages. The change from one stage to another are represented with the help of differential equations and the proportionality constants are estimated with the help of observed data from documented studies. The changes in stages are illustrated graphically. Those who never go for screening progress through the same stages of cancer invasion but do not benefit from medical interventions. However some of these women may be screened at a later date and benefit from medical interventions. While this model appreciates this phenomenon, the number of women who undergo this late /accidental screening has been assumed negligible and hence are not included in this mathematical model. The total number of women with undiagnosed HPV is denoted by W where $W(t_0) = 87241$

f) Undiagnosed Dysplasia

The number of women with undetected/ undiagnosed Dysplasia is denoted by $w_0(t_0)$ which is assumed to be at constant up to timet_s. Let $w_0(t)$ be the number of women at Undiagnosed Dysplasia at any time $t > t_s$ and $w_0(t_0) = 43621$

The rate of change in undiagnosed dysplasia is therefore;

$\frac{dw0(t)}{dt} = \alpha_7 [q - r]$ *(Eq 26)*

and $t > t_l$

$t_l$is the level off time when there are no more women available for progression to dysplasia stage.

$\alpha_7$is the progression factor of HPV from normal cells to w_0.This constant depends on; virulence of HPV subtype, general health status of the cervix and health behavior of the client.

$q$is the proportion of women eligible for screening

r *is* the proportion of screened women with undiagnosed Stage 1cervical cancer.

The undiagnosed dysplasia stage progresses to be stage 1 of undiagnosed cervical cancer

Undiagnosed cervical cases-In this case $W(t_0) = 872418$ and using the values from the observeddata:$w(t_0) = 43621$; $w(t_1) = 43621$;$w(t_2) = 87242$, $w(t_3) = 348967$ w; $w(t_4) = 348967$. The pattern was analyzed and found similar to the diagnosed stages.

g) Undiagnosed Dysplasia

The number of women with undetected/ undiagnosed dysplasia is denoted by $w_0(t_0)$ which is assumed to be at constant up to timet_s. Let $w_0(t)$ be the number of women with undiagnosed dysplasia at any time $t > t_s$ and $w_0(t_0)$=43621

The rate of change in undiagnosed dysplasia is therefore;

$d\,w_0(t)/dt = \alpha_7[q - r]$ *(Eq 27)*
and$t > t_l$
$t_l$is the level off time when there are no more women available for progression to Dysplasia stage.
$\alpha_7$is the progression factor of HPV from normal cells to w_0.This constant depends on; virulence of HPV subtype, general health status of the cervix and health living behavior of the client.
q is the proportion of women eligible for screening
r is the proportion of screened women with undiagnosed stage 1cervical cancer.
The undiagnosed dysplasia stage progresses to be stage 1 of undiagnosed cervical cancer.

h) Undiagnosed Stage 1

Let the Initial number of women with undiagnosed stage 1 be denoted by $w_1(t_0)$ which is assumed to be at constant up to time t_s. Let $w_1(t)$ be the number of women at undiagnosed stage 1 at any time $t > t_s$and $w_1(t_0)$= 43621.
The change in the proportion of women with undiagnosed stage one cancer at any given time is
$d\,w_1(t)/dt = \alpha_{16} w_0 - \beta_6 w_1$ *(Eq 28)*
Where;
$\alpha_{16}$is the progression factor from undiagnosed dysplasia to undiagnosed stage1,
$\beta_6$is progression factor from undiagnosed stage one to undiagnosed stage 2.

i) Undiagnosed Stage 2

The initial number of women at undiagnosed stage 2, be denoted by $w_2(t_0)$ which is assumed to be at constant up to timet_s. Let $w_2(t)$ be the number of women at Undiagnosed stage 2 at any time $t > t_s$ and $w_2(t_0)$= 87242
and the boundary condition is ;
$dw_2(t)/dt = 0$ when $0 \le t \le t_s$ and $w_2(t_0) \le 87242 \le w_2(t)$. *(Eq 29)*
Thus, the rate of change in the proportion of women with undiagnosed stage 2 is therefore,
$dw_2(t)/dt = \alpha_{17} w_1 - \beta_7 w_2$ *(Eq 30)*
Where
$\alpha_{17}$is a constant dependent on progression factor from undiagnosed stage 1 to undiagnosed stage 2
$\beta_7$is a constant that depends on the progression factor from undiagnosed stage 2 to undiagnosed stage 3.

j) Undiagnosed Stage 3

The initial number of women at undiagnosed stage 3 be denoted by $w_3(t_0)$which is assumed to be at constant up to time t_s. Let $w_3(t)$ be the number of women at undiagnosed stage 3 at any time $t > t_s$ and $w_3(t_0)$ = 348967. The boundary conditions therefore is,
$w_3(t)/dt = 0$when$0 \le t \le t_s$and $w_3(t_0) \le 348967 \le w_3(t)$
The rate of change of the proportion of women with Undiagnosed stage 3
$dw_3(t)/dt = \alpha_{18} w_2 - \beta_8 w_3 - \beta_9 w_3$ *(Eq 31)*
Where
$\alpha_{18}$is a constant dependent on progression factor from undiagnosed stage 2 to undiagnosed stage 3
$\beta_8$is a constant that depends on the progression factor from undiagnosed stage 3 to undiagnosed stage 4.
$\beta_9$is a constant of a factor representing death at stage 3.

k) Undiagnosed Stage 4

The initial number of women at undiagnosed stage 4 be denoted by $w_4(t_0)$ which is assumed to be at constant up to time t_s. Let $w_4(t)$ be the number of women at undiagnosed stage 4 at any time $t > t_s$.
$w_4(t_0)$=348967
$w_4(t)$/dt= $\alpha_{19} w_3 - \beta_{10} w_4$ *(Eq 32)*
α_{19} is a constant dependent on progression factor from undiagnosed stage 3 to undiagnosed stage 4
$\beta_{10}$is a constant of a factor representing death at stage 4.The growth patterns for both diagnosed and undiagnosed status in the population were identical hence yielding similar Matlab™ curves. However a difference was observed at the starting point as the initial values that are estimated from the WHO/ICO report taking 2010 as the base year for the respective stages.

Death from Cervical Cancer

Some of the women are permanently removed from the model through death denoted by *(z)*. Let the initial number of women deaths as a result of cervical cancer is denoted by $Z(t_0)$which is assumed to be at constant up to time t_s.Let $Z(t)$ be the number of women who die from both diagnosed and undiagnosed cervical cancer at any time $t > t_s$. . The boundary and the rate of change is therefore,
$\frac{dZ(t)}{dt}$=0, when$0 \le t \le t_s$ and $Z(t_0) \ge 2000 \le z(t)$ *(Eq 33)*
Death as a result of undiagnosed cervical cancer
$z_2 = \beta_{12} w_3 + \beta_{14} w_4$ *(Eq43)*
$z_3 = \beta_5 m_4 + \beta_4 m_3$. *(Eq 44)*
$Z\,(Total\ Deaths\ from\ cervical\ cancer) = z_2 + z_3$ *(Eq 45)*
The proportion of death at any one time is dependent on the women available to die from cervical cancer. The number of women infected with HPV and at different stages of cervical cancer at any time in the country can be estimated approximately.

5. Discussion

The results of this mathematical model show that the epidemiological trends of cervical cancer in Kenya can be mathematically explored. The various Matlab™ output graphs show the trends of the population of HPV infected women in different compartments over time. The resulting decrease in numbers over time of pre-cervical cancer stage never really goes to zero. This can be explained by the possibility of part of the population of women with pre-cancer state experiencing natural clearance of the HPV infection while others progress to stage 1 of cervical cancer. The results are similar to those of Lee & Tameru (2012) who demonstrated a decrease in susceptible, HPV infected and without treatment as well as a decrease in compartment of women with treatment interventions after diagnosis with HPV infection. The untreated compartment had an initial increase followed by a decrease with time. This may be attributed to the death rates which increase with disease progression. The earlier stage(stage 1 and stage 2) of

disease has lower death rate in comparison to the late stages(Stage 3 and stage 4).The epidemiological trends of cervical cancer in Kenya is comparable to results of HIV epidemiology (Simwa and Pokhariyal 2003) in East Africa which show that HPV /cervical cancer has a non zero prevalence and hence a long term epidemiological disease.

6. Conclusion

In this paper a dynamic time varying model for estimating control variables and changes in trends therein has been developed. Baseline data set adapted from WHO/ICO and published reports were used to test the model. These initial conditions form the basis for further investigation into the typography of cervical cancer in Kenya as well as prediction of the trends that cervical cancer is likely to take. The model is dynamic in the sense that it can be adjusted over the time of investigation. The model predicted reasonable estimates of real life expectations of progression of both diagnosed and undiagnosed cervical, death from cervical cancer as well as possible epidemiological trends taking into consideration the impact of the various interventions available. However given the inherent uncertainty against any inputs of mathematical models, the outputs need to be compared with observable epidemiological data.

7. Future Scope

There is need to develop a model covering the wider scope of Africa as a continent in cervical cancer as well as develop a model that accounts for change in detection process.

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