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# Surface Response Modeling of the Variations between Percentage Death and Prevalences for TB/HIV Co-Infection Rate

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***Abstract*****—** *In this work, the co-infection of HIV and TB, and the subsequent number of deaths caused by this is introduced and modelled. Literature on this has also been extolled and properly reviewed from the internet. The almost impossibility of obtaining this sort of materials for this work for many countries limits the work to one country (South Africa): Materials for the validation of the work were obtained from the internet only for South Africa (WHO, 2007). Surface plotting was made with the model by varying the interactions between percentage number of deaths, percentage HIV prevalence, percentage TB notification and time duration. It was revealed that in a country such as South Africa, as HIV and TB diseases propagate in the patients there are serious interactions between percentage HIV prevalence and percentage TB notification (fig. 1), percentage HIV prevalence and time duration (fig. 2), and percentage TB notification and time duration (fig. 3) as the death toll caused by the two diseases increase. The relationship between the movements of the 3 parameters (i.e. percentage number of deaths, percentage HIV prevalence and percentage TB notification) is clearly seen in another kind of 3D plot of figure 4. This work will help the HIV-AIDS workers and those studying the mechanisms of co-infection of HIV and TB in their researches around the world*.

***Keywords*****—** *Prevalences, deaths, TB/HIV, co-infection rates, surface response, modeling*.

## I. INTRODUCTION

There has been this believe that most people who have T.B will have HIV or vice versa. Observations from HIV and T.B patients in hospitals show that this believe is almost true and so there has been mathematical models from different authors on T.B and HIV co-infections [1], [2]. Deterministic, stochastic, compartmental use of differential equations and probabilistic models have all been used for the investigation into the joint HIV and T.B epidemics in some countries. But none have used statistical (surface response) modeling and this is what this work intends to use. Tuberculosis is a bacterial disease caused by m. tuberculosis (tubercle bacilli). T.B is the leading cause of death among people infected with HIV. Transmission of T.B occurs by airborne or spread of infectious droplets. The droplets are produced by a person with sputum smear-positive T.B of the lungs [3]. T.B is acquired through "interaction" with infectious individuals. Interactions that include primarily the sharing of a common "closed environment". Once infected, a person stays infected for many years, possibly latently-infected for life. Two billion people, about one-third of the world's total population were estimated to be infected with TB in 2006 [4]. HIV, the Human immunodeficiency virus is the etiological agent responsible for the acquired immunodeficiency syndrome (AIDS). HIV is not casually transmitted. There are multiple modes of HIV transmission including sexual intercourse, sharing needles with HIV infected persons or via HIV-contaminated blood transfusion [5]. Infants may acquire HIV at delivery (birth) or through breast feeding if the mother is HIV positive. HIV severely weakens the immune system. Hence, it makes people highly vulnerable to invasions by a great number of infectious agents including my-bacterium, the etiological agent responsible for T.B [6]. There is along variable latent period associated with HIV infection and the onset of HIV-related diseases including AIDS in adults. As infection progresses, immunity declines and patients tend to become more susceptible to 'common' or even rare infections. In many societies, HIV and TB treatments are common today and the uses of drugs have altered the joint dynamics of TB and HIV [7].

About one third of 39.5 million HIV-infected people worldwide are co-infected with T.B (34 - 50 percent of individuals living with HIV are expected to develop TB [8]. Many TB carriers who are infected with HIV are 30 to 50 times more likely to develop active TB, than those without HIV [8]. The HIV epidemic has significantly impacted the dynamics of T.B. In fact, one-third of the observed increases in active T.B cases over the last five years can be attributed to the HIV epidemic [8]. For individuals infected with HIV, the presence of other infections, including T.B tends to increase the rate of HIV replication. This acceleration may result in higher levels of infection and rapid HIV progression to the AIDS stage [9]. The potential implications on the joint dynamics of HIV and T.B will be explored in this work

It is important to investigate the effect of HIV and T.B co-infection and the resultant death of the patient so that it will be seen if there can be any way to solve the incurable HIV disease through the curable TB disease. It is also important to see if a common medication can them be administered for the co-infection. The alarming rate of death from TB and HIV co-infection on patients makes this study imperative.



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The problem of HIV and T.B co-infection on the patients with its alarming rate of death is a serious concern for the world today in general and nations in particular coupled with the fact that HIIV/AIDS is incurable when T.B is super-imposed on it, it becomes complex and the tendency of it being incurable is very high. The problem therefore is how to solve the combined disease of HIV/T.B infection using mathematical models so that if understood and workable, medication can follow.

Although the negative impact of the synergetic interactions between T.B and HIV have caused worldwide concern, only a few statistical or mathematical models have been used to explore the consequences of their joint dynamics at the population level. There are plenty of single disease dynamic models. A significant number focus on T.B or on the transmission dynamics of HIV/AIDS [10]. There are a few T.B/HIV co-infection models [11]. Kirschner developed a cellular model that described HIV-1 and T.B co-infections inside a host. [12] developed a nonlinear mathematical model with the population divided into four sub classes: the susceptible, TB infective, HIV infective, and AIDS patients. Their model focused on the transmission dynamics of HIV and treatable T.B in populations of varying sizes. [13] studied HIV/T.B joint dynamics using actuarial methods. [14] developed models for the joint dynamics of HIV and TB using numerical simulations to estimate parameters and predict the future transmission of TB in the United States.[14] predict the potential impact of HIV on the probability and the expected severity of TB outbreaks using a discrete event simulation model.

According to [15]. Tuberculosis has been a leading cause of death in the world for centuries. During the period from 1945 to 1985, because of improved medical treatment and hygiene practices, the number of cases of TB steadily declined.

However, from 1985 through 1992, in the US alone, there were over 50,000 extra cases of death by pathogen-induced diseases worldwide and 3.1 million in 1996. It is believed this recent increased incidence is in large part due to HIV. Other factors certainly include an increase in poverty levels as well as the dismantling of TB control programs. Also, since this resurgence of TB in 1985, TB has been called the "main opportunistic disease for HIV" [16]. It is clear that each of these diseases can have a profound impact on the other [9].

First it has been shown [17], [18] that HIV-infected individuals are at an increased risk of developing TB in the active form. Second, there is an increasing interaction between those individuals at high risk for TB and those at high risk for HIV: drug users, homeless and inner-city minorities [19]. TB is the most common HIV-related complication worldwide [20]. HIV infected individuals are not only at a greater risk of acquiring TB (as much as 500 times the normal chance in HIV-negative individuals), but reactivation of latent TB infection is greatly increased due to the fact that the very sells that hold the latent TB in check (the $CD4^+$ T lymphocytes) are precisely the cells that are rendered dysfunctional in HIV-infected individuals [7]. TB decreases the number of $CD4^+$T cells thereby interfering with the best predictor of AIDS survivability [21]. This is important, because the $CD4^+$ T cells are the cells that not only become infected with HIV, but orchestrate the immune response against both TB and HIV, as well as other pathogens. Treatment of TB infection, in the case of non-resistant strains, is well developed. The most common treatment regime is a combination of isoniazid, rifampin and pyra-zin amide for 2 months, followed by isoniazid and rifampin for at least 4-7 months until all the bacteria have been completely cleared [5]. If adhered to properly, the cure rate is almost 1000. There are many problems, however, with administering a treatment regime that has such a long duration, the main one being compliance. In many cases, patients do not complete therapy, and this not only causes a rebound in the individual's TB, but also aides in the formation of mutant strains that are drug resistant [6]. These "first-line" drugs are the best defense against TB, and in their loss of use, due to multi-drug resistance to some or all of the drugs, treatment becomes difficult, costly, or even impossible with a cure rate of only 600. Treatment of HIV is not so clear cut, as is true of most viral infections. Presently multiple antiviral agents administered in combination serve only to slow the progression to AIDS, but as yet, there is no cure.

## II. Materials and Method

The materials for the study of HIV prevalence, TB notification and the corresponding number of death accruing from them cannot be found in a developing country like Nigeria. Therefore, you need to browse the internet to obtain the empirical data for this work.

The method is to model the co-infection and interaction from first principle using the logic of interactive reaction and algebra of HIV prevalence, TB notification and corresponding number of death accruing from them. When this model is developed and established, data from the internet will be browsed for, to test the validation of the developed model and far reaching conclusions and inferences will be made.

Parameters used include

(1) HIV prevalence
(2) TB notification
(3) Death rate.

### *2.1 Development of Models*

There have been models from different authors on the co-infection of HIV and TB, but the approach here differs from those found in the literature so far. Here, focus is given to the joint dynamics of HIV and TB in the pseudo-competitive environment at the population level. Although the negative impacts of the synergetic interaction between TB and HIV have caused worldwide concern, only a few statistical or mathematical models have been used to explore the consequences of these joint dynamics at the population level. There are plenty of single disease dynamic models. There are a few of TB/HIV co-infection models e.g. [12]. Their models focused on the transmission dynamics of HIV and treatable TB in population of varying sizes.

TB is the leading cause of death among people infected with HIV. Transmission of TB occurs by air-born spread of infectious droplets. TB is acquired through interaction with



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infectious individuals, interactions that include primarily the sharing of a common 'closed environment'. Once infected the person stays infected for many years, possibly latently-infected for life.

A simple statistical (surface response) model has been developed below for the interaction between HIV and TB epidemics.

*2.2 Assumptions*

(1) Death rate is a constant (i.e. not affected by HIV prevalence or TB notification: the natural death).

$$Y = a_0 \quad (2.1)$$

(2) Death rate is proportional to the interaction between HIV prevalence ($x_1$) and TB notification ($x_2$) i.e.

$$Y = a_3 x_1 x_2 \quad (2.2)$$

(3) Death rate is jointly: (i) linearly proportional to HIV prevalence (ii) proportional to the square of HIV prevalence i.e.

$$Y = a_1 x_1 + a_4 x_1^2 \quad (2.3)$$

(4) Death rate is jointly: (i) linearly proportional to TB notification (ii) proportional to the square of TB notification i.e.

$$Y = a_2 x_2 + a_5 x_2^2 \quad (2.4)$$

Combining 1 to 4 gives;

$$Y = a_0 + a_1 x_1 + a_2 x_2 + a_3 x_1 x_2 + a_4 x_1^2 + a_5 x_2^2. \quad (2.5)$$

*2.3 Data Collection*

Data for percentage HIV prevalence, percentage TB notification and their corresponding percentage number of death and year were browsed for, from the internet for South Africa as shown in table I below. Such corresponding data were pretty difficult to obtain for other countries which would have made a good comparative study for the countries.

*2.4 Curve-Fitting and Surface Plotting*

Surface plotting of percentage number of death vs. percentage HIV prevalence with percentage TB notification were plotted. Their interactions with themselves and time would be also plotted using MATLAB 7.9 package. Accuracy of the plots was measured by the statistical goodness of fit of the plot as the coefficients of the model were declared within 95% confidence bound.

Also, a 3D plot was made to see the direct effect of percentage death, percentage HIV prevalence and percentage TB notification

## III. Results and Discussion

*3.1 Result Presentation*

The results of the computer analysis and data plots are as shown below. (Fig. 1 – Fig. 4).

TABLE I. Percentage mean death VS percentage HIV prevalence and corresponding percentage TB notification and infection period (UNAIDS/WHO, 2007).

| (Year) t Time | t | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| %HIV($x_1$) | $H_x$ | 1.9 | 2.5 | 3.3 | 3.7 | 4.35 | 4.75 | 5.2 | 5.75 | 6.0 | 6.2 | 6.35 | 6.4 | 6.4 | 6.38 | 6.4 | 6.43 |
| %TB($x_2$) | $T_y$ | 0.07 | 0.075 | 0.08 | 0.085 | 0.09 | 1.0 | 1.08 | 1.13 | 1.2 | 1.28 | 1.36 | 1.48 | 1.56 | 1.67 | 1.72 | 1.80 |
| %Mean Death (Y) | $D_z$ | 4.65 | 4.95 | 5.80 | 6.50 | 6.97 | 7.25 | 7.45 | 7.56 | 7.68 | 7.78 | 7.86 | 7.92 | 7.98 | 8.03 | 8.07 | 8.12 |

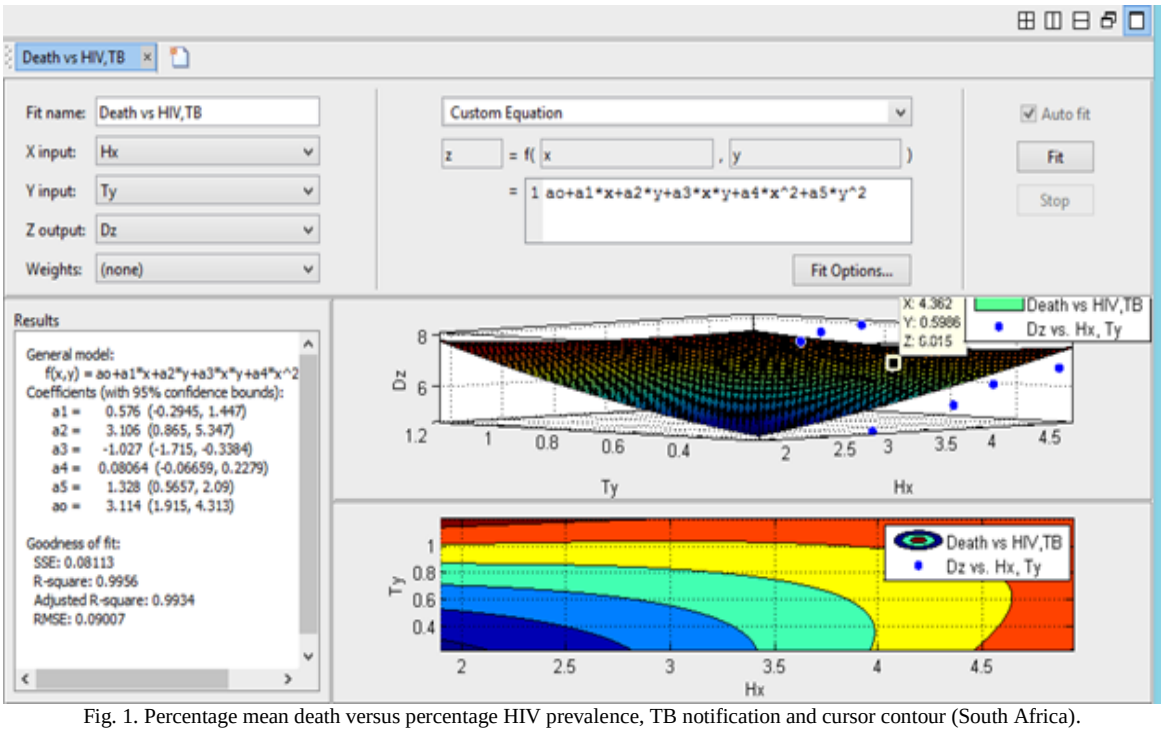


Fig. 1. Percentage mean death versus percentage HIV prevalence, TB notification and cursor contour (South Africa).



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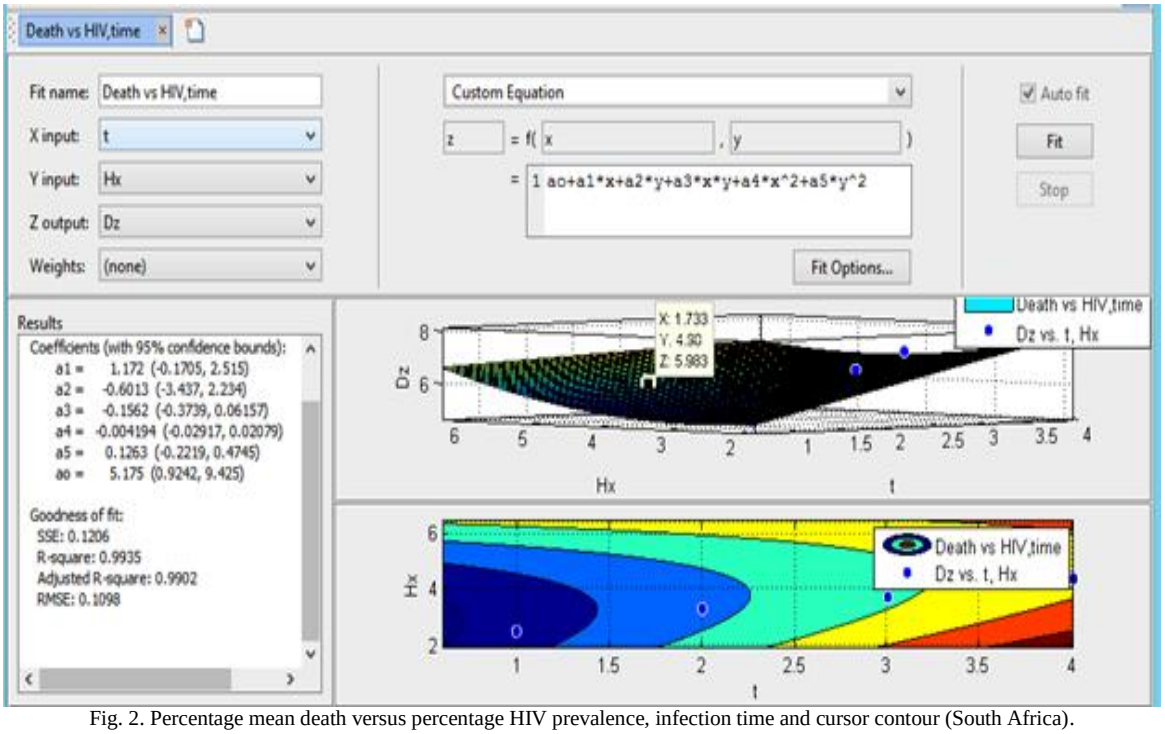

Fig. 2. Percentage mean death versus percentage HIV prevalence, infection time and cursor contour (South Africa).

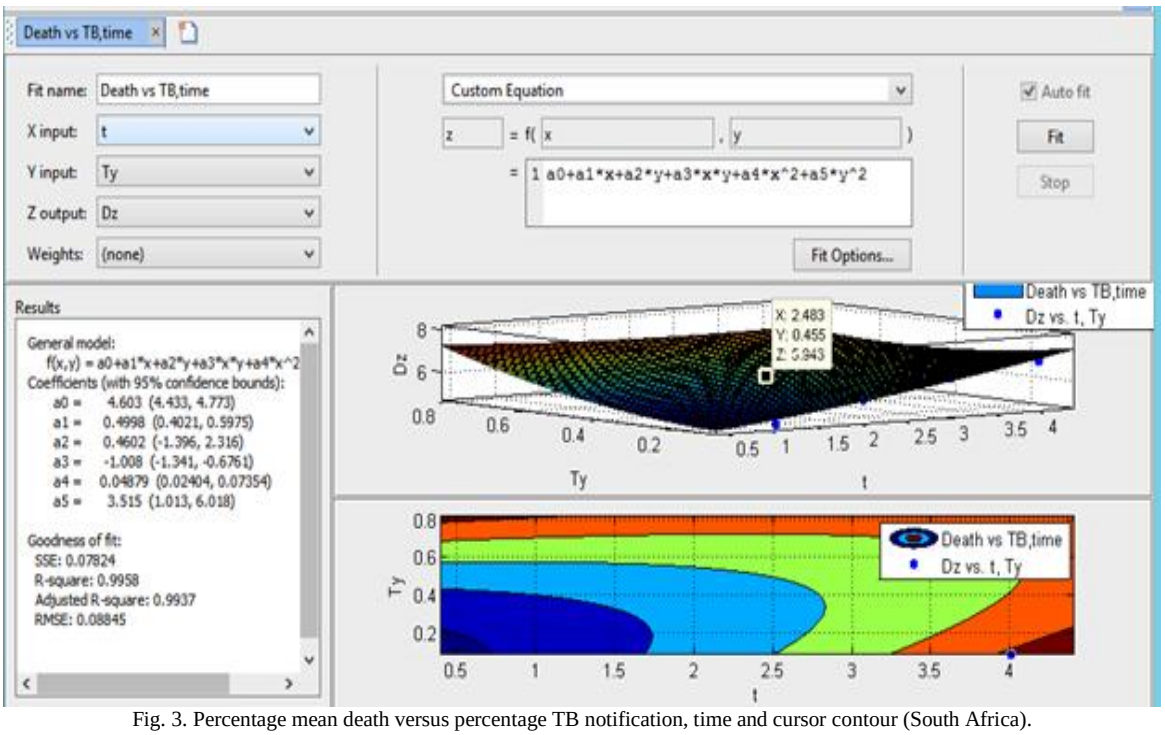

Fig. 3. Percentage mean death versus percentage TB notification, time and cursor contour (South Africa).

*3.2 Discussion*

In Fig. 1, a surface plot of percentage number of death vs. percentage HIV prevalence and percentage TB notification were made. Its cursor contour appears directly below it and shows high degree of interaction between percentage HIV prevalence and percentage TB notification as the two diseases spread in a patient (those bands of curves). The statistical goodness of fit shows 99.56% accuracy as the coefficients of the model are declared

In Fig. 2, a surface plot of percentage number of deaths, percentage HIV prevalence and time duration shows a mesh plot, as the cursor contour below it shows high degree of interaction between percentage HIV prevalence and time duration (bands of curves in the plot of the contour). The



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statistical goodness of fit reveals a 99.35% accuracy as it declares the coefficient of the model therein.

In Fig. 3, another surface plot of percentage number of deaths vs. Percentage TB notification with time duration is made. The mat-like plot has a cursor contour below it that is also having high degree of interaction between percentage TB notification and time (bands of curved lines in the contour plot). The statistical goodness of fit reveals a 99.58% accuracy as it declares the values of the coefficients of the model.

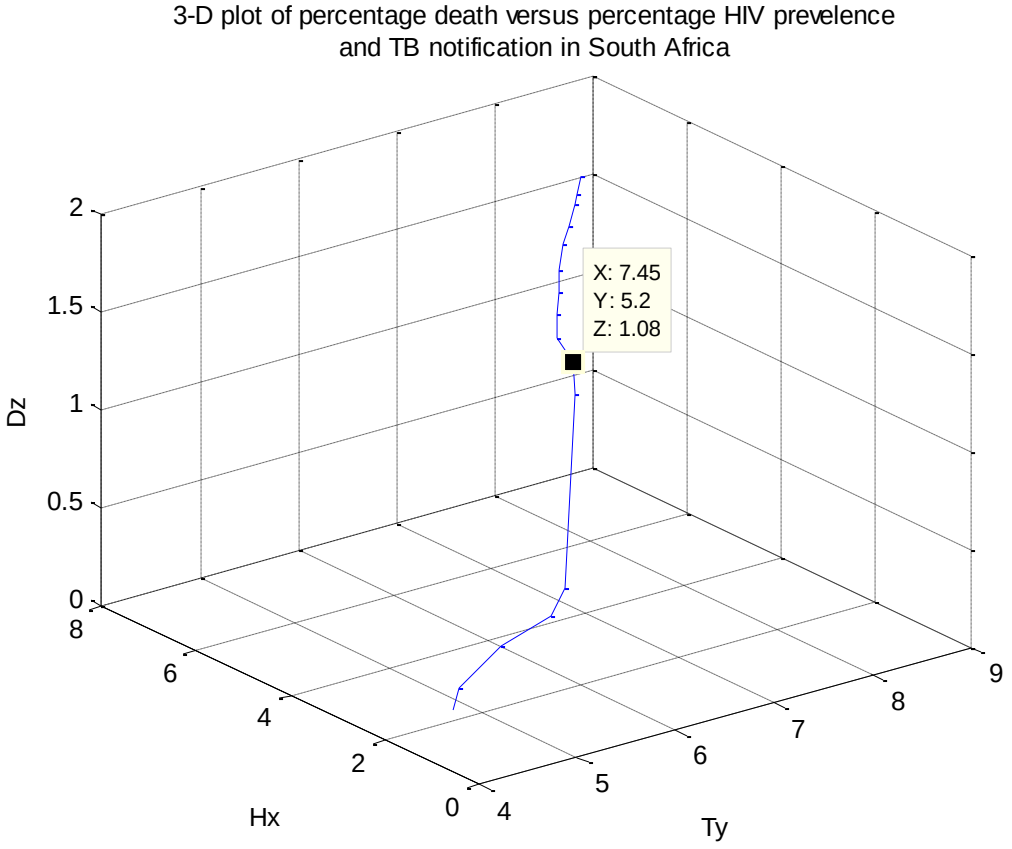


Fig. 4. 3-D plot of percentage death versus percentage HIV prevalence and TB notification in South Africa.

Fig. 4 shows another kind of 3D plot of percentage number of deaths, percentage HIV prevalence and percentage TB notification. The plot shows the mechanical characteristic movements of percentage number of deaths, percentage HIV prevalence and percentage TB notification in South Africa.

At every point in the graph you can read percentage number of deaths, percentage HIV prevalence and the corresponding percentage TB notification.

## IV. Conclusion

In this work, the co-infection of HIV and TB, and the subsequent number of deaths caused by this is introduced and modelled. Literature on this has also been extolled and properly reviewed from the internet. The almost impossibility of obtaining this sort of materials for this work for many countries limits the work to one country (South Africa): Materials for the validation of the work were obtained from the internet only for South Africa (WHO, 2007). Surface plotting was made with the model by varying the interactions between percentage number of deaths, percentage HIV prevalence, percentage TB notification and time duration. It was revealed that in a country such as South Africa, as HIV and TB diseases propagate in the patients there are serious interactions between percentage HIV prevalence and percentage TB notification (Fig. 1), percentage HIV prevalence and time duration (Fig. 2), and percentage TB notification and time duration (Fig 3) as the death toll caused by the two diseases increase. The relationship between the movements of the 3 parameters (i.e. percentage number of deaths, percentage HIV prevalence and percentage TB notification) is clearly seen in another kind of 3D plot of figure 4.This work will help the HIV-AIDS workers and those studying the mechanisms of co-infection of HIV and TB in their researches around the world.

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