LONG TERM TRANSMISSION OF THE HIV/AIDS EPIDEMIC
A SYSTEM DYNAMICS APPROACH
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INTRODUCTION

The computer simulation model presented in this paper, facilitates the quantitative understanding of the population dynamics of epidemic outbreaks of AIDS. This model provides public health authorities with the predicted consequences of different available control strategies, thus helping to select optimal policies and better choice of intervention strategies. As the AIDS epidemic grows to alarming proportions in many parts of the world, causing social and economic losses, widespread disruption and repression of community life, it is important to have an understanding about the underlying causes of the disease and to predict the future trend of the development of the epidemic.

System Dynamic methodologies have been applied to develop AIDS/HIV models. This method facilitates the understanding of the relationship between the underlying structure of the epidemic and the behavior generated by this system.

The purpose of the research is two-fold. First, analyzing the structure and the behavior of the epidemic with the help of System Dynamics, secondly, testing the models with various parameters in order to evaluate an information system and recommend a policy design.

The model, not only illustrates the various stages in the epidemic, but also the level of seniority among the infected population. It investigates the effect of variation in the transition probability, which facilitates the progression to infectiousness and transition to AIDS.

The model described in the article encompasses various non-infectious latencies*, which may have a significant impact on the development of the epidemic. However, the duration of non-infectious latency is not known and suspected to be many months, the main model portrays four different durations which ensures the different behavioral patterns generated by the various latencies in the development of the epidemic.

The main model is used to illustrate the importance of the invisible infectiousness based upon the distribution of the incubation latency**. It explores the effect of infectiousness (where the antibody titres are reduced to low and barely detectable levels in the initial stages of the disease) with various medical testing methodologies (Gallo et al. 1984). This might enhance the economic relevance of testing policies, which enables the evaluation of cost benefit analysis in the health services.

A simplified model has also been constructed to mirror the peoples perception of the epidemic, with respect to changes in sexual practices, and the time taken by the public to realize the severity of the disease and to either eliminate or modify the activities that promote the transmission of the disease. These aspects are characterized by response time and forgetfulness in the models.

The comparison between the simplified model and the main model presented in this paper creates a setting for synthetic data analysis in order to evaluate an information system. This analyzes the effect of simplified assumptions as a basis for policy design.

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* *the interval between the date of exposure and the point of conversion to infectiousness is denoted as non-infectious latency.*

** *the time interval from the exposure to full blown AIDS.*

IMPORTANCE OF MODELING THE AIDS/HIV EPIDEMIC.

Dynamic aspects of the spread of the disease exhibit the behavioral pattern which is caused by an underlying structure. Understanding of the underlying structure has major importance in designing and implementing the effective policies.

The epidemic system which we are looking into, embodies some major properties which enhances the applicability of System Dynamics as the simulation tool. The system exhibits the causal relationship that exists between the variables. Dynamic tendencies arise from the causal structure of the system. This two ways causation of the structure is explained by feedback loops. In this particular system, time delays are one of the crucial determinants of the dynamic behavior (delays in information and physical flows). Nonlinearities are believed to be important in explaining the system behavior. The nonlinearities cause the feedback loop of the system to vary in strength. In general, a model composed of several feedback loops linked nonlinearly produces a wide variety of complex behavioral pattern. Therefore nonlinearities and time delays of the epidemic system can be handled by System Dynamics models with great ease.

The informations which are retrieved from the reality of the spread of the disease could be interpreted in different ways, based on the paradigms of the decision models. The data which are retrieved from the reality and which plays a major role in the spread of the disease has the potentiality of being discarded, when it is proved to be insignificant by the statistical analysis. On the other hand, information obtained from the actual state of the epidemic may result in changes in the perception of the current state of the spread which would lead to an alteration in the factors determining the rate of transmission of the epidemic.

An information system, required for the control of the AIDS epidemic will have to be based upon a simplified model of the epidemic and the more or less frequent estimation of parameters, which are considered to be essential to the spread of the disease. All the more, there is reason to test the validity of such models, to investigate under what circumstances they are applicable, and under what circumstances their results will lead policy makers to wrong conclusions.

This can be done in a synthetic data experiment where we let our main model represents the actual state of the epidemic and simplified versions of this model represent the models applied for policy design purposes.

The simplified models which use the estimation/simulation process mirror many methods, to explain and/or predict the behavior of an HIV/AIDS epidemic. Some of these consist of pure statistical trend extrapolations (Rees M, 1987). They are generally based upon the assumption that a very simple model (one well suited for statistical estimation purposes) appropriately portrays the structure underlying the epidemic behavior. Typically, this may be a purely positive feedback loop model portraying exponential growth. Such a model will be based upon the estimation of the doubling time, and will be applied to the analysis of the earlier development of the epidemic. On the other hand, it may be a purely negative feedback loop model that exhibits an exponential approach towards an equilibrium or a steady state. Such a model will be based upon an estimation of the half-life time, and will be applied to the analysis of the later part of the epidemiological development. Such exponential models may be transformed logarithmically into a linear form, ideal for statistical estimation. The models applied for short term prediction of the AIDS epidemic tend to be log-linear (Tillett and MacEvoy, 1986) and unsuitable for long term dynamic considerations. Changes in the dynamics are often caused by the corresponding changes in the significance of the underlying structural elements.

By using more advanced, statistical models, we may try to anticipate the behavior of the epidemic to its full extent. These models are typically based upon statistical density functions, such as the Weibull, Gamma, or other distributions, more or less appropriately justified with reference to the underlying structure of the epidemic. These distributions are assumed to represent the uncertainties related to the latencies of the epidemic (Baily, Lui, Lawrence, Morgan, 1986).

As our understanding of the underlying structure grows, we require more elaborate models of greater complexity, which are not as well suited for standard estimation procedures. As the degree of complexity is increasing, the need for simulation models becomes more obvious. The modeling paradigm that states; "Identify the simplest possible model that can explain an observed phenomena" necessarily constitutes a framework for the development of simulation models as well as analytical models. In particular, this is the case when we approach a reality with which we are not familiar and where the estimation of parameter values are inhibited by;

- estimators that do not reflect the inherent complexity underlying the epidemic; and/or

- a few, uncertain observations, characterized by delays.

These two models presented here are mainly based upon the assumption that the infected persons go through a multiple stage disease, where each stage is characterized by a certain level of infectivity and a mean latency. People are expected to leave each stage according to an exponential first order delay. Altogether this causes the latencies to be distributed among the population characterizing some distribution, related to the gamma or Weibull distribution.

In line with Anderson, we also conclude that after AIDS has been diagnosed the individual concerned are unable to infect further susceptibles (Anderson et al. 1986). It is also assumed that all the seropositive individuals develop AIDS before death. At present, recovery from AIDS is not possible and there is no need for a stage of recovery in the models.

THE MAIN MODEL

The main model is initialized with 30000 sexually passive individuals, 60000 susceptibles*, 50 noninfectious negatives** and 10 infectious positives† . The model assumes that the recruitment rate originates only from sexually mature individuals, so that the susceptibles and the infected population enhance the recruitment rate with an average time taken to attain the sexual maturity (see Fig. 1).

The Intensity of Infection

Intensity of infection* is a crucial parameter in determining the rate of infection of the epidemic and it is influenced by two other factors.

- Biological factor
- Habitual factor

In our model the intensity of infection (ß) is assigned with the value of 0.4 (component determined by the biological factor), which is modified by the effect of prevalence on ß. The habitual factor constitutes two other components:

Peoples reaction to sero-prevalence

- pattern of reaction; Graph 1. views the effect of sero-prevalence on the intensity of infection. It shows the pattern of reaction, where 50% of the sero-prevalence eliminates the promiscuity among the sexually active individuals.

Response time: time taken for the people to react to the changes in sero-prevalence.

- forgetfulness; the sexually active individuals tend to forget the severity of the epidemic, as the sero- prevalence reaches the saturation point. This in turn, promotes high risk sexual activities among the individuals, that may propagate the epidemic. We have chosen to apply various time lengths of forgetfulness in order to study the effect of the change in sexual practices in the development of the epidemic.

The indicated effect of the sero-prevalence on the intensity of infection (ß) is obtained if;

- there had been an immediate response to a change in sero-prevalence in the form of a corresponding change in the promiscuity among the individuals.

- there is no adaption of previous sexual behavior as a consequence of forgetfulness.

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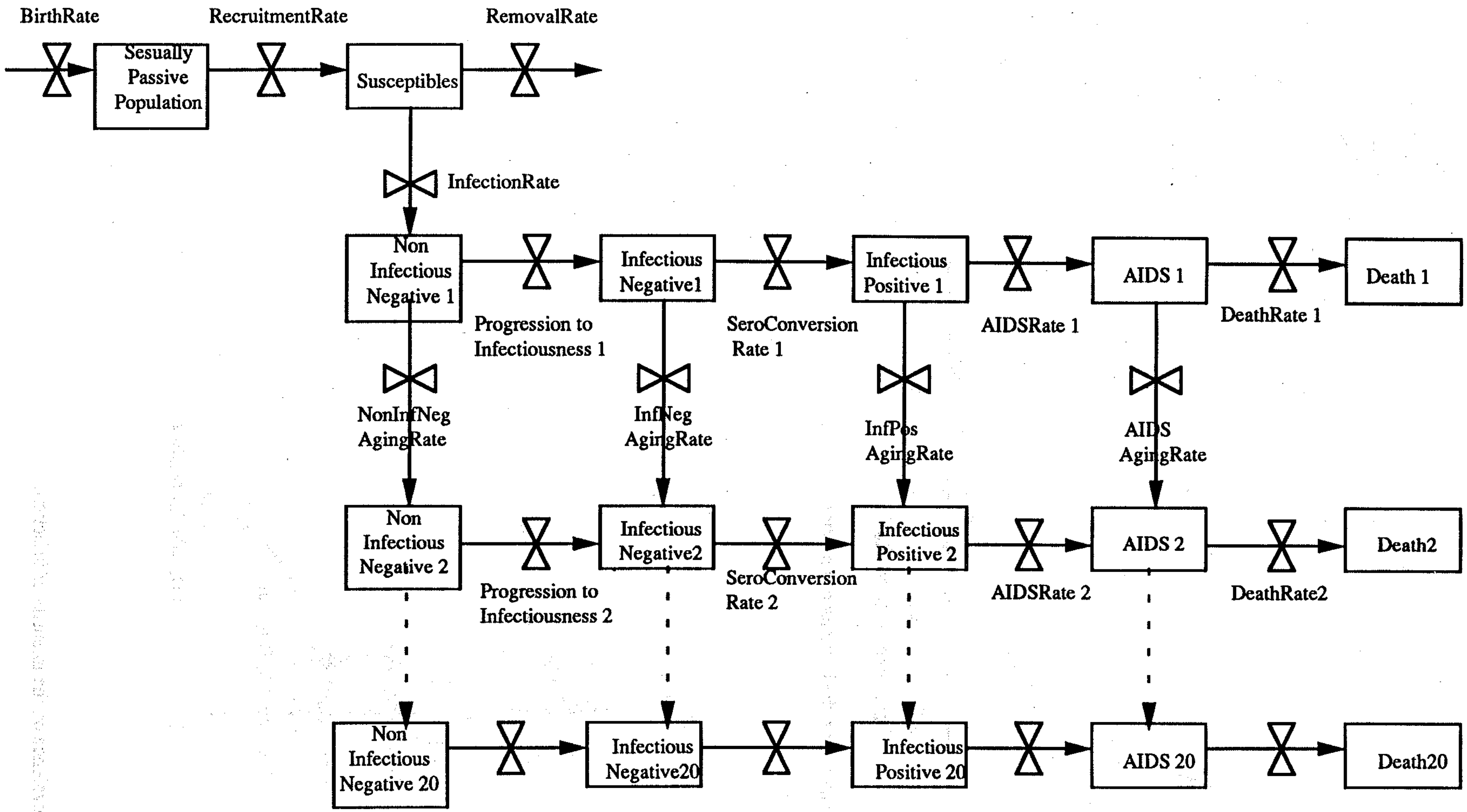
* *Uninfected individuals who on exposure to the agent can be infected.*

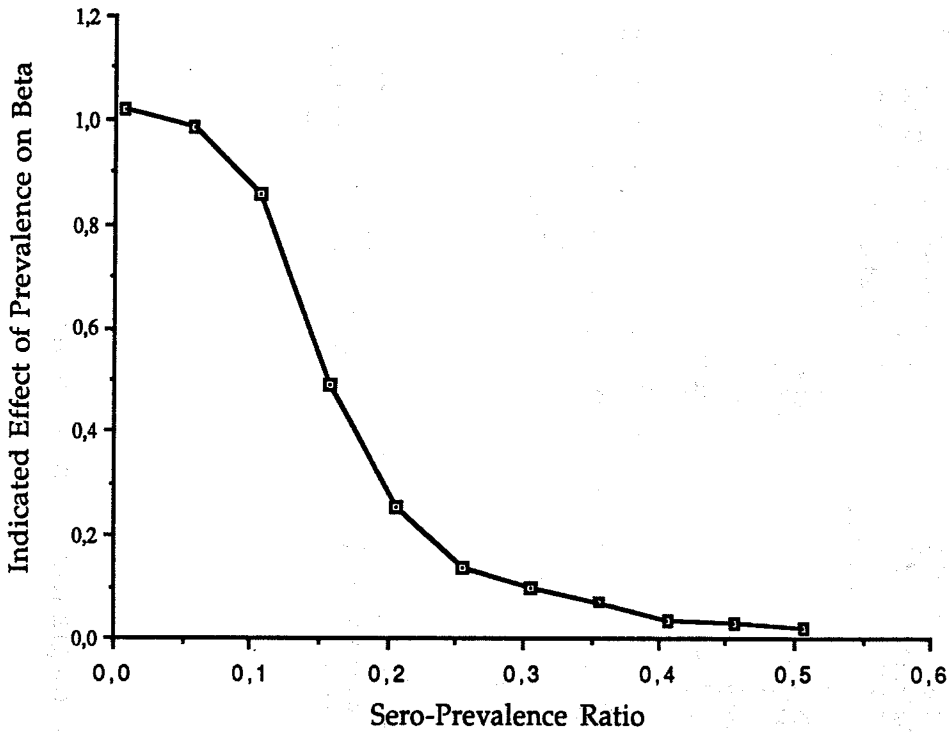
** *Individuals who are infected, sero-negative and are not infectious.*

† *Infected individulas who are infectious and have gained a detectable level of antigens in the blood.*

* *Intensity of infection is denoted as ß in our model.*



Fig, 1. Stock and flow diagram of the main model



Graph 1. Effect of sero-prevalence on the intensity of infection

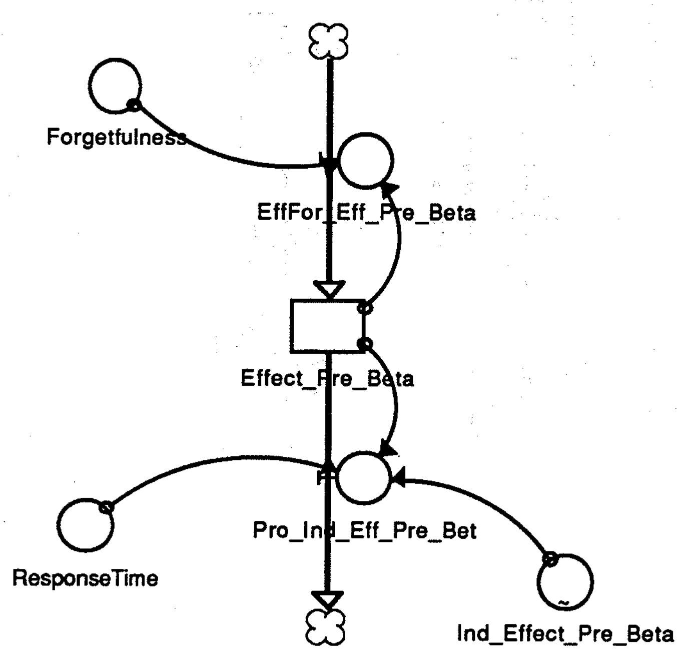


FIG 2. The effect of sero-prevalence on the intensity of infection.

The effect of prevalence of ß is partly characterized by a first order goal seeking behavior, whereby it moves with the delay represented by the response time, towards the effect indicated by the current prevalence. The indicated effect is portrayed as a function of sero-prevalence in graph 1. For instance, if the sero-prevalence increase by an step input, the actual effect of prevalence on the intensity of infection settles at the indicated level after a while. This goal seeking behavioral pattern is clearly displayed in Exhibit 1.

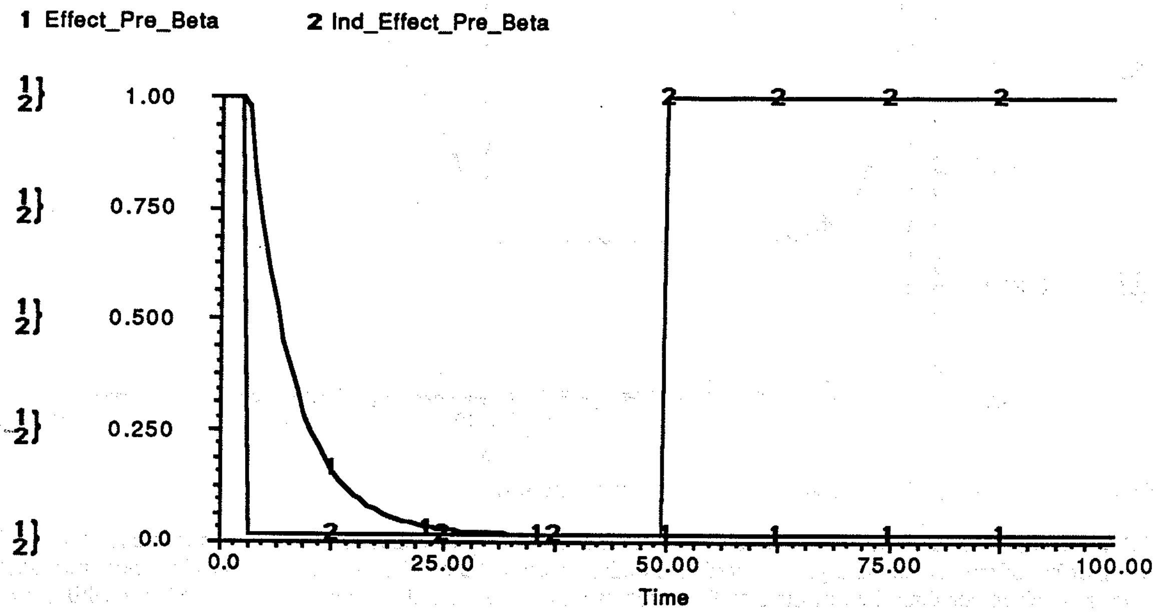


Exhibit 1. A response of promiscuity to sero-prevalence

The process of forgetting, counteracts the process of responding to the seroprevalence. People have a tendency to fall back to old habits as the time and generations pass on. In our model, this is portrayed by another first order goal seeking process that tend to bring the effect of prevalence on the intensity of infection back to its original level (biologically determined ß 0.4) with the certain delay corresponding to the duration of forgetfulness. Longer the duration of forgetfulness, slower the process of returning back to the point of departure. So if we assume that the seroprevalence increases by an step input and people respond relatively quickly to the new level of seroprevalence, and forget relatively slowly, the indicated level of promiscuity represented by ß is almost reached before forgetfulness sets in. This indicated effect on the ß is active over a longer period of time before it reestablishes the original level of promiscuity.

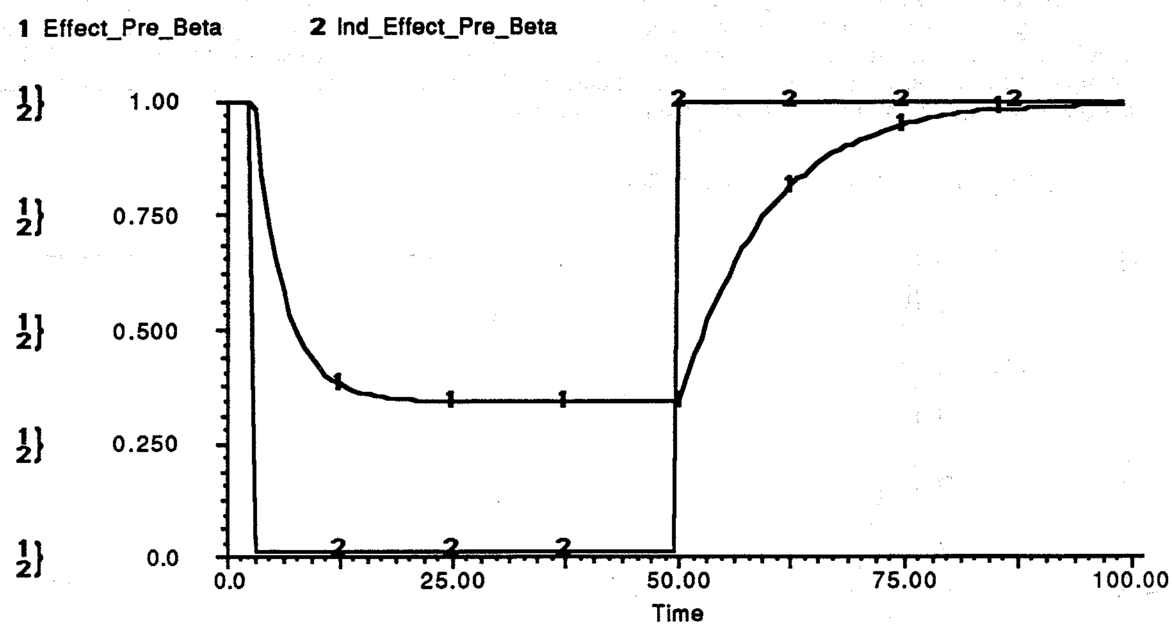


Exhibit 2. A response of promiscuity to sero-prevalence and forgetfulness.

Exhibit 2. displays the behavioral pattern of the actual effect of prevalence on ß as the forgetfulness sets in. The actual effect of prevalence on ß goes towards the indicated effect before the forgetfulness sets in, since the response time is much lower than the duration of forgetfulness and it reaches the equilibrium state after a while. As the indicated effect on ß increases, the first order negative feedback characterized by a delay of forgetfulness dominates, thereby increasing the actual effect gradually to its original value.

Some of the recent works predict (May, Anderson, McLean 1988) that the initial condition of the HIV infection would be long, of the order of many decades. The simulation of our main model has been carried out over a wide time horizon, range of 150 years. We perform the investigation of the effects of various non-infectious latencies characterized by 5%, 10%, 15%, 20% of the incubation time.

THE SIMPLIFIED MODEL

Purpose and aggregate structure of the simplified model

The simplified model which has been described in this paper represents the perception of reality. The purpose of developing this simplified model is to test the models which have been developed by other researchers (Bailey 1985; Dangerfield 1988; Anderson 1988) to predict the trend of the development of the epidemic and thereby utilizing these predictions in decision making.

The development of such models have an important role to play in assisting quantitative understanding and thus facilitating a better choice of intervention strategies. This simplified model also facilitates a setting for synthetic data analysis that may be utilized to evaluate the effect of such simplified models in policy design.

There are only two significant simplifications made in the simplified model.

•It disregards the seniority stratification within each stage of the disease and the corresponding distribution of transfer probabilities, i.e the inverse of latencies; and

•It disregards the existence of infectious negatives.

The simplified model describes the stages through which an individual may pass, the susceptibles, noninfectious negatives, infectious positive and AIDS (see Fig 3). This model assumes that infected individuals remain noninfectious for a certain period of time before they convert to infectiousness.

In a work done by Anderson (Anderson et al. 1986), using an exponentially increasing rate function the Weibull incubation period, he emphasizes " In interpreting these fitted mean values it is important to bare in mind that the data being fitted lie in the lower tail of the fitted distribution, while the mean is estimated on the assumption that the fitted distribution will work equally well in the upper tail on which it is highly dependent. Estimation of the mean from data in the lower tail alone is likely to be unreliable".

Therefore, the simplified model has been tested under four different conditions (which are used to investigate the different phases of the development) in order to analyze its behavior and compare them with the main model. The various conditions are applied to verify whether the parameter estimated from the simplified models in the observed development differs from the development generated by the main model.

The conditions that are applied to test the behavior of the model are based upon the observed sero-prevalence (Total seropositive*) and the observed incidence of the infection (sero-conversion rate**) with a perceived delay of 3 years and 5 years, respectively.

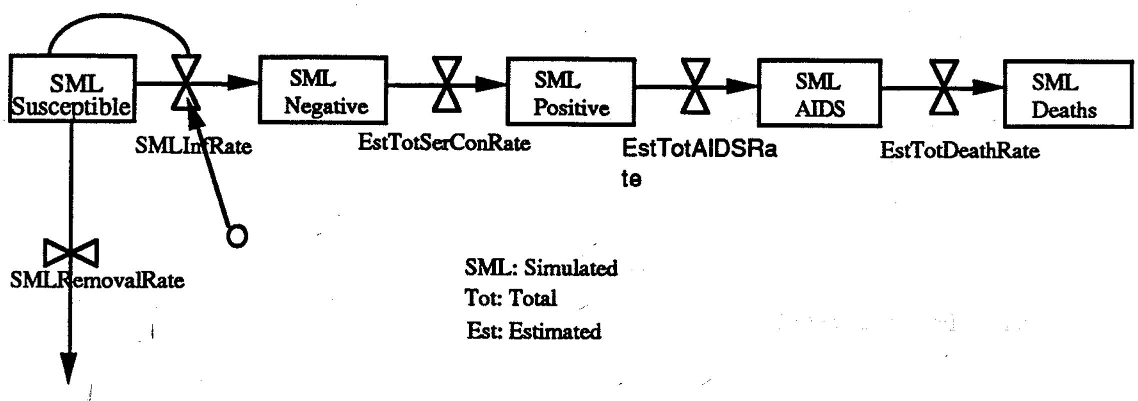


FIG 3. Stock and flow diagram of the simplified model

A SIMPLIFIED SYNYHETIC DATA ANALYSIS

In the symplified data analysis, the main model and the simplified version of the model are simulated in paralall. The simplified model is initialized and parameterized, by estimation based upon observation from the main model.

We may consider the simplified model as comprising two kinds of assumptions; (Davidsen 1983).

- fundamental ones, and

-modifiable ones, initial parameter values.

So, in addition to the fundamental assumptions, we must provide a description of initial and parameter values which are retrieved and estimated, i.e. the link between the main model and the simplified model (see fig. 4).

As a result of this process we obtain two sets of behavior:

• one from the main model; and

• one from the simplified model.

By comparing these two, we may draw a conclusion with respect to the quality of the simplified model, the consequences applying this as a basis for policy design, and conditions under which such an application may be warranted.

* *Infected population who are infectious and have gained a detectable levels of antigens in the blood.*

** *The rate at which the sero-negative individuals convert to sero-positive.*

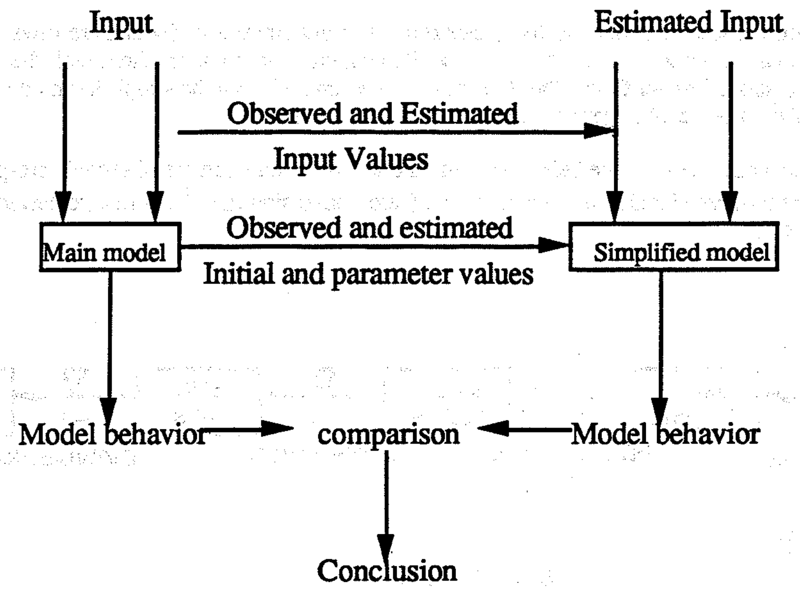


FIG 4. A simplified synthetic data analysis

CONCLUSION

General discussions from the experiments

We have carried out a simplified version of a synthetic data experiment, based upon a main model of an AIDS epidemic. From this main model, we have derived a simplified model, corresponding to the one frequently encountered, in scientific literatures, and used for public decision making, and policy design purposes. The process of simplification has been straight forward so that we may clearly attribute the differences between the behavior of the main model and the simplified model, to the corresponding differences in the underlying systems structure. In this process, the group of invisibly infectious individuals have been included in the negative population (denoted as SML_Neg in the simplified model) and we ignore the seniority of the infected individuals and thereby the distribution of the probability to progress through the stages of the disease, associated with their seniorities. Both of these simplifications are made because of our inability to identify, or determine the seniority of the infectious individuals. As a consequence we cannot expect a model that contains such information to be initialized and parameterized effectively, by an information system. Therefore, it is common to introduce the kind of simplification that we have made. By comparing the behavioral mode generated by these two models, and analyzing the consequences of applying the simplified version of synthetic data analysis as a basis for policy design, we have identified a very complicated intimate inter-relationship between the development of the main model (portraying the actual state of the epidemic) and the simplified model. Our findings are summarized as follows.

A simplified model of reality may serve more or less effectively as a basis for policy design, depending upon the circumstances prevailing in reality and how they are represented in the model and upon the initialization and parameterization of the model, i.e the information system design to support the application of the model. Moreover, the relative effect of these factors are significantly influenced by the timing (phase of the development of the epidemic) of the usage of the model as a policy tool.

First of all, our experience has indicated that reality plays a major role: The degree of forgetfulness, characterizing the tendency to fall back to promiscuous behavior, has two separate effects on the behavior of the simplified model. On the one hand, the forgetfulness influences the behavior of the simplified model directly, as a part of its structure and on the other hand, the forgetfulness influences the behavior of the main model. This behavior determines how the simplified model is initialized and parameterized and thereby the behavioral pattern generated by the model.

Our investigations reveal, as the simplified model is being initialized, parameterized and applied, the direct effect of forgetfulness with respect to the behavior of the model, is less obvious in the earlier stages of the epidemic. We see this clearly by comparing the effect of forgetfulness on the behavioral patterns.

Moreover, our investigations exclude the significance of the forgetfulness with respect to the behavior of the main model as it becomes more prominent over time. Therefore, the main models influence upon the behavior of the simplified model could potentially become more significant. In fact, the initialization, parameterization and application of the simplified model differed its behavior over time. We observe that the behavior of the simplified model is increasingly influenced by the values inherited by the main model, by parameterization. In the earlier phases of the epidemic, the initial values do not seem to have a great influence, but some parameter values seem to be more significant. For instance, the significance may be attributed to the intensity of infection which varies between a wide range, in the main model while the significance of seropositive latency is quite moderate.

From our investigations, we may conclude that, if the simplified model is applied at an early phase in the development of the epidemic (until sero-conversion peaks), then the direct influence of the forgetfulness, as a part of the model itself, has a great significance. If the simplified model is applied at a later phase of the epidemic, then the indirect influence caused by the parameterization is the most significant one.

Having described the changes in the significance of parameter values applied, caused by the discrepancy in forgetfulness, we may identify a similar shift in the significance of the initial values particularly in the transition from the behavioral modes of the simplified models.

As the effect of forgetfulness and the corresponding significance of the parameterization and initialization fluctuate, the validity of the simplified model as a basis for policy design, is sensitive to the timing of its initialization, parameterization and application.

The application of the simplified model as a basis for decision making policy design discussed so far, are based upon the utilization of the simple synthetic data analysis. But the more complex synthetic data analysis may give us a better basis for drawing conclusions as to the effect using the simplified model in policy design. The complex synthetic data analysis requires a simulation approach, that is not well supported by any of the software packages, commonly used for system dynamic purposes.

To carry out the modeling, The modeling language Stella has been chosen. This contains a powerful set of graphically based tools for constructing System Dynamic models.

<u>REFERENCE LIST</u>:

JOURNALS:

Anderson. 1975 "Population dynamics of infectious disease"

Anderson. and May. 1987 "Transmission dynamics of HIV infection"

Bailey. 1985. "Simplified modeling of the population dynamics of HIV/AIDS"

Davidsen, P. 1983 "System Dynamics: A useful paradigm in the design of Managerial Information System".

Davidsen, P. Sterman,J. Richardson, G. 1990: "A petroleum life cycle model for the United States with endogeneous technology, exploration, recovery and demand"

Fauci, A. 1988. " HIV infectivity and mechanism of pathogenesis"

Forrester, J. 1983. "System Dynamics - Future opportunities"

Gonzalés og Koch. 1988. "On the role of Transient for the prognostic analysis of the AIDS epidemic"

Gallo, R. 1988 "The AIDS virus"

Sterman, J. 1986 "Testing behavioral simulation models by direct experiment"

Richardson, G. 1981. " Statistical Estimation of Parameters in a Predator-prey model: An Exploration Using Synthetic Data".

Valerie, I. 1988. "Mathematical modelling of transmission dynamics of HIV infection and AIDS".