Stochastic Modeling of HIV Dynamics within an individual and its management

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Outline

• Brief overview
• Statement of the problem
• Objectives of the study
• Significance of the study
• Methodology
• Expected outcomes
Brief overview

- Why model HIV/ AIDS
- Interaction of the HIV virus and the immune system of an infected person
- Why stochastic processes
Problem statement

• Eradication of the HIV virus is not attainable with the current available drugs and now the focus is the management and control of the virus progression in an infected person.

• The allocation of the limited budget by the Government to combat the disease.
Research Objectives

Main objective
• To develop stochastic models for the study of HIV internal viral dynamics and its management.

Specific objectives
• Formulate a model for the Virus – host interaction
• Formulate stochastic Models for the progression of the disease
• Formulate a HIV Management Cost (HMC) Model
• Formulate a Cost Benefit Analysis (CBA) Model
Significance of the study

- Stochastic models for the management of the HIV epidemic
  - The analysis of the models will show what treatment combination is effective at what disease state.
  - The cost model will help the government and donors make informed decisions about resource allocation.
Methodology

Framework for stochastic processes

- Mathematical Modeling
  - Stochastic Process
    - Deterministic Models
    - Continuous Time Discrete State
      - DTCS
      - CTCS
      - DTDS
      - Branching Processes
        - Pure Death
          - Birth and Death
            - Emigration
              - Birth, Death and Immigration/Emigration
                - Probability Distributions
          - Pure Birth
            - Immigration
Methodology (Cont)

objective 1: HIV – Host interaction dynamics

- Deterministic Modeling
- Stochastic Process Modeling
- Continuous Time Discrete State
- Birth – Death Processes
- Birth, Death and Immigration
- Difference-Differential Equations
- Partial Differential Equations
- Probability Distributions

- Statistical Modeling
- Markov Chains
- Immigration
HIV virus – host Interaction dynamics

\[ \dot{X} = \lambda - \delta X - \alpha \beta XV \\
\dot{V} = \gamma \mu V - \beta XV - \omega N \kappa Y \\
\dot{Y} = kY \]

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## Possible transitions in HIV - host interactions

<table>
<thead>
<tr>
<th>Event</th>
<th>Population components (X,Y,V) at t</th>
<th>Population components (X,Y,V) at (t, t + Δ)</th>
<th>probability of transition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Production of uninfected cell</td>
<td>(x - 1, y, v)</td>
<td>(x, y, v)</td>
<td>λΔt</td>
</tr>
<tr>
<td>Death of uninfected cell</td>
<td>(x + 1, y, v)</td>
<td>(x, y, v)</td>
<td>δ(x + 1)Δt</td>
</tr>
<tr>
<td>Infection of uninfected cell</td>
<td>(x + 1, y - 1, v + 1)</td>
<td>(x, y, v)</td>
<td>β(x + 1)(v + 1)Δt</td>
</tr>
<tr>
<td>Production of virions from the dying infected cell</td>
<td>(x, y + 1, v - 1)</td>
<td>(x, y, v)</td>
<td>κN(y + 1)Δt</td>
</tr>
<tr>
<td>Introduction of Virons due to re-infection because of risky behaviour</td>
<td>(x, y, v - 1)</td>
<td>(x, y, v)</td>
<td>γΔt</td>
</tr>
<tr>
<td>Death of virons</td>
<td>(x, y, v + 1)</td>
<td>(x, y, v)</td>
<td>μ(v + 1)Δt</td>
</tr>
</tbody>
</table>
The Master equation for Virus-Host interaction

\[ P'_{x,y,v}(t) = -\{\lambda + \delta x + \alpha \beta x v + \mu v + \kappa y + \gamma\} P_{x,y,v}(t) + \lambda P_{x-1,y,v}(t) + \delta (x + 1) P_{x+1,y,v}(t) + \alpha \beta (x + 1)(v + 1) P_{x+1,y-1,v+1}(t) + N \omega \kappa (y + 1) P_{x,y+1,v-1}(t) + \gamma P_{x,y,v-1}(t) + \mu (v + 1) P_{x,y,v+1}(t) \]
The Lagrange Partial Differential Equation

\[
\frac{\partial G}{\partial t} = \{(z_1 - 1)\lambda + (z_3 - 1)\gamma\}G + \left(1 - z_1\right)\delta \frac{\partial G}{\partial z_1} + \left(\omega N z_3 - z_2\right)\kappa \frac{\partial G}{\partial z_2} \\
+ \left(1 - z_3\right)\mu \frac{\partial G}{\partial z_3} + \alpha \beta (z_2 - z_1 z_3) \frac{\partial^2 G}{\partial z_1 \partial z_3}
\]
Moments of X(t), Y(t) and V(t) from the pgf

1. \[ \frac{dx}{dt} = \lambda - \delta x(t) - \alpha \beta x(t)v(t) \]

2. \[ \frac{dy}{dt} = \alpha \beta x(t)v(t) - \kappa y(t) \]

3. \[ \frac{dx}{dt} = \gamma + \omega N \kappa y(t) - \alpha \beta x(t)v(t) \]
Methodology (Cont)

objective 2: HIV virus progression dynamics

- Mathematical Modeling
- Stochastic Process
  - DTCS
  - CTCS
  - Continuous Time Discrete State
  - Birth – Death Processes
  - Pure Death
  - Birth and Death
  - Emigration
  - Birth, Death and Immigration/Emigration
  - Probability Distributions
- Deterministic Models
  - DTDS
  - Markov Chains
  - Pure Birth

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HIV progression dynamics

- We will assume that the clinical course of untreated HIV infection proceeds through five states:

  **State 1:** (VL ≤ 400 cp/ml & CD4 < 200x10^6 cells/µL);
  **State 2:** (VL ≤ 400 cp/ml & CD4 > 200x10^6 cells/µL);
  **State 3:** (VL > 400 cp/ml & CD4 > 200x10^6 cells/µL);
  **State 4:** (VL > 400 cp/ml & CD4 < 200x10^6 cells/µL);
  **State D:** Absorbing state; (death of the patient).
Expected outcomes

- Stochastic model for Virus –host interaction
- Markov models to describe the disease internal progression in an infected person
- Transition probabilities that describe the various stages of the disease
- A Disease Management Cost (DMC) model
- Cost Benefit Analysis (CBA) model
- Future Scientific Research
Thank you