A Delay Differential Equation Model of HIV Testing and Treatment

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Abstract

We develop a compartmental model for evaluating HIV testing and treatment scenarios. A system of coupled delay differential equations is used to represent three stages of HIV infection, plus the fourth stage of symptomatic AIDS. The model is implemented using a system dynamics approach and numerical analysis is used to study the stability of solutions.

Parameters

Variable	Description
x_{iU}	undiagnosed stage i HIV infection
x_{iHU}	stage i HIV infection with high viral load
x_{iLU}	stage i HIV infection with low viral load
x_{iHT}	initial high viral load stage i HIV infection under treatment
x_{iLT}	initial low viral load stage i HIV infection under treatment
y_U	undiagnosed AIDS
y_K	diagnosed but untreated AIDS
y_T	AIDS under treatment

Parameter	Description	Estimated Value
Transmission Rates [new infections / 100 persons · year]		
β_{iU}	undiagnosed i^{th} state HIV	0.25, 0.1, 0.25
β_{iHU}	diagnosed, untreated, high viral load progression i^{th} state HIV	0.25, 0.1, 0.25
β_{iLU}	diagnosed, untreated, low viral load progression i^{th} state HIV	0.25, 0.05, 0.15
β_{iHT}	treated, initial high viral load progression i^{th} state HIV	0.25, 0, 0
β_{iLT}	treated, initial low viral load progression i^{th} state HIV	0.25
β_{AU}	undiagnosed AIDS	0.25
Death Rates [deaths / person · year]		
δ	non-AIDS related causes	0.00657
δ_A	death rate from AIDS	0.00002
Stage Durations / Time Delays [months]		
τ_{iU}	undiagnosed i^{th} state HIV	2, 78,
τ_{iHU}	diagnosed, untreated, high viral load i^{th} state HIV	2, 78, 30
τ_{iLU}	diagnosed, untreated, low viral load i^{th} state HIV	2, 78, 30
τ_{iHT}	treated, high viral load i^{th} state HIV	2, 78, 30
τ_{iLT}	treated, low viral load i^{th} state HIV	2, 78, 30
τ_{AU}	undiagnosed AIDS	1
τ_{AK}	untreated AIDS	1
Fraction of HIV Positive Tested		
μ_i	stage i	0.0, 0.01, 0.02
Fraction with Low Viral Load Pre-treatment		
λ_i	stage i	0.0, 1.0, (0.60, 0.90)
Fraction Treated		
α_{iH}	high viral load in stage i	0.0, 0.0, 1.0
α_{iL}	low viral load in stage i	0.0

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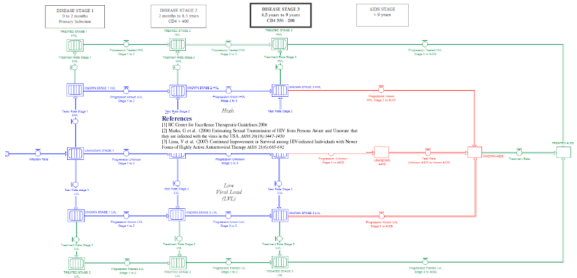
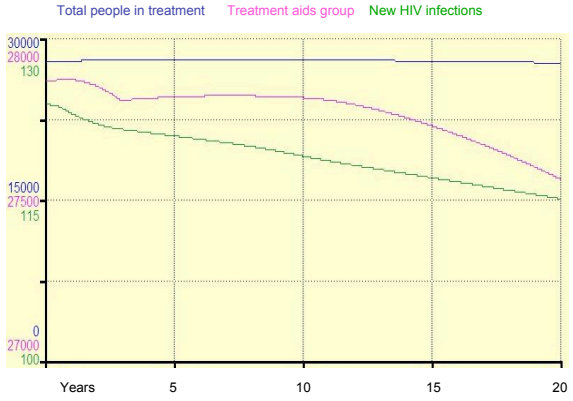
The Model

- Newly infected patients move through 4 disease stages
- 30% of infected individuals remain unaware of their disease status
- Remaining patients may receive testing and treatment at any time
- Tested patients may have high or low viral loads
- Boxes are stocks of unknown infected, known infected, treated and AIDS patients
- Hashed boxes incorporate time delays
- Arrows with valves show transmission, testing and treatment rates
- Blue, green and red portions of the graph represent untreated, treated and AIDS patients, respectively



Simulation



Scenario

- The simulation was initiated and run until it achieved a relatively stable population
- Only those in stage 4 (AIDS) were treated in this initial phase
- Following initalisation, the top 40% of stage 3 infections with the highest viral load were sent to treatment.
- This scenario was used to evaluate the impact of an HIV treatment strategy whereby patients with high viral load and CD4 counts in the range of 200 to 350 are referred for treatment.
- This corresponds with current treatment recommendations by the British Columbia Centre for Excellence.

Conclusions

Using delay differential equation models we are able to explicitly take into account the length of time patients spend in specific stages of HIV infection. The model demonstrates how different disease stages give rise to latency in the overall disease dynamics.

Future Directions

- Estimates for the parameters of the model will be further refined.
- A stochastic DDE model will be developed to take into account individual variability in disease progression.
- The complex dynamics of the model will be studied to understand better the role played by latency in the model, and stability of solutions of the system of coupled DDEs.

References

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