Stochastic Hepatitis C model - conditions for disease extinction

Vuk Vujović, Marija Krstić

University of Niš
Faculty of Sciences and Mathematics
Department of Mathematics

8th European Congress of Mathematics
Portorož, Slovenia, June 20-26, 2021
Hepatitis C

- Hepatitis C belongs to a group of infectious disease that affects the liver and was discovered in 1989.
- Hepatitis C is a silent epidemic, because symptoms can take long time to be visible.
- Hepatitis C spreads only through exposure to an infected persons blood.
- There is no vaccine against Hepatitis C so far.

Figure: Methods of transmission of Hepatitis C.
Introduction and Motivation

M. Imran, M. Hassan, M. Dur-E-Ahmad, A. Khan

A comparison of a deterministic and stochastic model for Hepatitis C with an isolation stage, Journal of Biological Dynamics 7(1)(2013) 276-301.

\[
\begin{align*}
\frac{dS(t)}{dt} &= \Pi + \omega R(t) - \lambda S(t) - \mu S(t), \\
\frac{dA(t)}{dt} &= \lambda S(t) - \left(\xi + \kappa + \mu + \delta_a\right) A(t), \\
\frac{dC(t)}{dt} &= \xi A(t) - \left(\alpha + \psi + \mu + \delta_c\right) C(t), \\
\frac{dQ(t)}{dt} &= \alpha C(t) - \left(\gamma + \mu + \delta_q\right) Q(t), \\
\frac{dR(t)}{dt} &= \kappa A(t) + \psi C(t) + \gamma Q(t) - \left(\omega + \mu\right) R(t),
\end{align*}
\]

\(S(0) = S_0, \ A(0) = A_0, \ C(0) = C_0, \ Q(0) = Q_0, \ R(0) = R_0\) - initial conditions.
Model parameters:
- \( \Pi \) - recruitment rate,
- \( \mu \) - natural death rate,
- \( \gamma \) - recovery rate of isolated individuals,
- \( \delta_a, \delta_c, \delta_q \) - disease-induced death rate for acute, chronic and isolated individuals, respectively,
- \( \xi \) - progression rate from the acute to the chronic stage of Hepatitis C,
- \( \alpha \) - isolation rate of chronically infected individuals,
- \( \kappa \) - natural recovery rate of acutely infected individuals,
- \( \psi \) - recovery rate of chronically infected individuals,
- \( \omega \) - progression rate of recovered individuals to susceptible individuals,
- \( \beta \) - effective contact rate,
- \( \eta, \zeta \) - modification parameter for infectiousness of acute and isolated individuals, respectively.

\[
\lambda = \lambda(t) = \beta \left[ \frac{\eta A(t) + C(t) + \xi Q(t)}{N(t)} \right], \quad t \geq 0 \quad \text{- the force of infection}
\]
Basic reproduction number:

\[ R_0 = \frac{\beta(\eta k_2 k_3 + \xi k_3 + \alpha \xi)}{k_1 k_2 k_3}, \text{ where } k_1 = \xi + \kappa + \mu + \delta_a, k_2 = \alpha + \psi + \mu + \delta_c, k_3 = \gamma + \mu + \delta_q \]

Disease-free equilibrium: \( E^0 = (S^0, A^0, C^0, Q^0, R^0) = \left( \frac{\Pi}{\mu}, 0, 0, 0, 0 \right) \)

The endemic equilibrium: \( E^* = (S^*, A^*, C^*, Q^*, R^*) \) where:

\[
S^* = \frac{1}{\lambda^*} \frac{k_1 k_2}{\xi} C^*, \quad A^* = \frac{k_2}{\xi} C^*, \quad Q^* = \frac{\alpha}{k_3} C^*, \quad R^* = \frac{1}{k_4} \left( \frac{k_1 k_2}{\xi} + \psi \right) C^* \quad \text{and} \quad \lambda^* = \beta \left[ \frac{\eta A^* + C^* + \zeta Q^*}{N^*} \right]
\]
V. Vujović, M. Krstić


Construction of stochastic model is based on procedure from [1].

\[
\begin{align*}
    dS(t) &= \left[ \Pi + \omega R(t) - (\lambda + \mu)S(t) \right] dt + \sigma_1 \left( S(t) - \frac{\Pi}{\mu} \right) dw_1(t) \\
    dA(t) &= [\lambda S(t) - k_1 A(t)] dt + \sigma_2 A(t)dw_2(t) \\
    dC(t) &= [\xi A(t) - k_2 C(t)] dt + \sigma_3 C(t)dw_3(t) \\
    dQ(t) &= [\alpha C(t) - k_3 Q(t)] dt + \sigma_4 Q(t)dw_4(t) \\
    dR(t) &= \left[ \kappa A(t) + \psi C(t) + \gamma Q(t) - k_4 R(t) \right] dt + \sigma_5 R(t)dw_5(t)
\end{align*}
\] (2)

- \( S(0) = s_0, \ A(0) = a_0, \ C(0) = c_0, \ Q(0) = q_0, \ R(0) = r_0 \) - initial condition,
- \( w(t) = (w_1(t), w_2(t), w_3(t), w_4(t), w_5(t), t \geq 0) \) - the five-dimensional standard Brownian motion defined on a complete probability space \((\Omega, \mathcal{F}, P)\),
- \( \sigma_i \ (i = 1, 2, 3, 4, 5) \) - arbitrary real constants
Existence and Uniqueness of Positive Solution

**Theorem 1**

For any initial value \((s_0, a_0, c_0, q_0, r_0) \in \mathbb{R}_+^2\), system (2) has unique global positive solution \((S(t), A(t), C(t), Q(t), R(t))\) for \(t \geq 0\).

**Sketch of proof**

- **Stopping time:**

  \[
  \tau_m = \inf \left\{ t \in [0, \tau_\varepsilon) : S(t) \notin \left( \frac{1}{m}, m \right) \lor A(t) \notin \left( \frac{1}{m}, m \right) \lor C(t) \notin \left( \frac{1}{m}, m \right) \lor Q(t) \notin \left( \frac{1}{m}, m \right) \lor R(t) \notin \left( \frac{1}{m}, m \right) \right\},
  \]

- **\(C^2\)-function \(V : \mathbb{R}_+^5 \to \mathbb{R}_+\):**

  \[
  V(S, A, C, Q, R) = S - 1 - \ln S + A - 1 - \ln A + C - 1 - \ln C + Q - 1 - \ln Q + R - 1 - \ln R.
  \]
Stability in Probability of $E_0$

**Question**

How does the intensity of noise affect the spread of Hepatitis C?

**Theorem 2**

Let the parameters of system (2) satisfy condition $R_0 < 1$ and

\[
2\beta\eta + \hat{a}\xi + \beta\zeta < 2k_1, \tag{3}
\]

\[
\alpha + \hat{a}\beta \left(1 + \frac{\zeta}{2}\right) < 2k_2, \tag{4}
\]

\[
\alpha + \beta\zeta \left(1 + \frac{\hat{a}}{2}\right) < 2k_3, \tag{5}
\]

\[
\beta\eta < k_1 + k_2, \tag{6}
\]

where $\hat{a}$ is an arbitrary positive number such that

\[
\hat{a} > \frac{2(\beta + \xi)}{k_1 + k_2 - \beta\eta}. \tag{7}
\]
Theorem 2 (extension)

Assume also that

\[ \sigma_1^2 < 2\mu, \]
\[ \sigma_2^2 < 2k_1 - (2\beta \eta + \hat{a}\xi + \beta\zeta), \]
\[ \sigma_3^2 < 2k_2 - \left( \alpha + \hat{a}\beta \left( 1 + \frac{\zeta}{2} \right) \right), \]
\[ \sigma_4^2 < 2k_3 - \left( \alpha + \beta\zeta \left( 1 + \frac{\hat{a}}{2} \right) \right), \]
\[ \sigma_5^2 < 2k_4. \]

Then the disease-free equilibrium of system (2) is stable in probability.
Sketch of proof

1. \( X = S - \frac{\Pi}{\mu} \)

2. \[
dX(t) = \left[ \omega R(t) - (\lambda + \mu)X(t) - \lambda \frac{\Pi}{\mu} \right] dt + \sigma_1 X(t) d\omega_1(t)
\]

3. \[
dA(t) = \left[ \lambda X(t) + \lambda \frac{\Pi}{\mu} - k_1 A(t) \right] dt + \sigma_2 A(t) d\omega_2(t)
\]

4. \[
dC(t) = \left[ \xi A(t) - k_2 C(t) \right] dt + \sigma_3 C(t) d\omega_3(t)
\]

5. \[
dQ(t) = \left[ \alpha C(t) - k_3 Q(t) \right] dt + \sigma_4 Q(t) d\omega_4(t)
\]

6. \[
dR(t) = \left[ \kappa A(t) + \psi C(t) + \gamma Q(t) - k_4 R(t) \right] dt + \sigma_5 R(t) d\omega_5(t)
\]

7. \( X(0) = S_0 - \frac{\Pi}{\mu}, \ A(0) = A_0, \ C(0) = C_0, \ Q(0) = Q_0, \ R(0) = R_0. \)
Introduction and Motivation  
The Model  
Existence and Uniqueness of Positive Solution  
Stability in Probability of $E_0$

Sketch of proof (extension)

Linearization procedure is based on procedure from [2].

\[
\begin{align*}
\dot{X}(t) &= \left[ -\mu X(t) - \beta \left( \eta \bar{A}(t) + \bar{C}(t) + \zeta \bar{Q}(t) \right) + \omega \bar{R}(t) \right] dt + \sigma_1 \bar{X}(t) d\omega_1(t) \\
\dot{A}(t) &= \left[ \beta \left( \eta \bar{A}(t) + \bar{C}(t) + \zeta \bar{Q}(t) \right) - k_1 \bar{A}(t) \right] dt + \sigma_2 \bar{A}(t) d\omega_2(t) \\
\dot{C}(t) &= \left[ \xi \bar{A}(t) - k_2 \bar{C}(t) \right] dt + \sigma_3 \bar{C}(t) d\omega_3(t) \\
\dot{Q}(t) &= \left[ \alpha \bar{C}(t) - k_3 \bar{Q}(t) \right] dt + \sigma_4 \bar{Q}(t) d\omega_4(t) \\
\dot{R}(t) &= \left[ \kappa \bar{A}(t) + \psi \bar{C}(t) + \gamma \bar{Q}(t) - k_4 \bar{R}(t) \right] dt + \sigma_5 \bar{R}(t) d\omega_5(t),
\end{align*}
\]  

- $V(\bar{A}, \bar{C}, \bar{Q}) = \bar{A}^2 + \bar{C}^2 + \bar{Q}^2 + a \bar{A} \bar{C}$
- $A = C = Q = 0$

\[
\begin{align*}
\dot{X}(t) &= -\mu \bar{X}(t) dt + \sigma_1 \bar{X} d\omega_1(t) \\
\dot{R}(t) &= -k_4 \bar{R}(t) dt + \sigma_5 \bar{R} d\omega_5(t),
\end{align*}
\]
Example

- Initial value: \( s_0 = 2000, \ a_0 = 200, \ c_0 = 600, \ q_0 = 120, \ r_0 = 100 \)
- The values of model parameters [3]:

\[
\begin{align*}
\Pi &= 0.12, \ \gamma = 0.18, \ \kappa = 0.2, \ \omega = 0.95, \ \mu = \frac{1}{21900}, \ \xi = 0.7, \ \alpha = 0.15, \ \psi = 0.05, \\
\delta_a &= 0.000233, \ \delta_c = 0.00233, \ \delta_q = 0.001667, \ \eta = 0.5, \ \zeta = 0.1, \ \beta = 0.136.
\end{align*}
\]

- Values of white noises: \( \sigma_1^2 = 0.00009, \ \sigma_2^2 = 0.102, \ \sigma_3^2 = 0.0169, \ \sigma_4^2 = 0.06, \ \sigma_5^2 = 0.005. \)
- Basic reproduction number: \( R_0 = 0.6454 < 1 \)
- Disease-free equilibrium point: \( E_0 = (2628, 0, 0, 0, 0) \)
Figure: Deterministic (black line) and 25 stochastic trajectories for acute individuals $A(t)$ of deterministic and stochastic models.
Figure: Deterministic (black line) and 25 stochastic trajectories for chronic individuals $C(t)$ of deterministic and stochastic models.
Figure: Deterministic (black line) and 25 stochastic trajectories for isolated $Q(t)$ (left) and recovered individuals $R(t)$ (right) of deterministic and stochastic models.
**Figure:** Twenty five stochastic trajectories for susceptible individuals $S(t)$. 
References


Thank you for your attention!!!