Modelling the Influence of Unhealthy Human Behaviour on the Spread of Zoonosis Disease that May Cause a Possible Future Pandemic

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Abstract. This paper addresses some strategies to improve the quality of management system in the laboratories by presenting models and methods for analyzing the effect of un-healthy human behavior on zoonosis disease spread and possible future pandemic. The possible future pandemic is modelled by a hypothetical mutated virus as a result of virus recombination. The variability of seven disease states among anima and humans are described as deterministic processes and modeled in the form of a well-defined initial value problem. The epidemic model has six disease state equilibria of which four are globally asymptotically stable and the others are locally asymptotically stable. Analyses show that: (i) to control the spread of disease means to control the effective rate of disease transmissions (ii) containing the disease in the animal world does not stop the spread of the implicated diseases in the human world. (iii) the spread of the mutant virus has a bigger magnitude than original in terms of the proportion of individuals acquiring the disease. (iv) reducing the contact among the animals will reduce the spread of the disease in the animal and human population but not stop the spread of the mutant virus. (v) social distancing programs reduce the number of human casualties.

1. Introduction
Most pandemics originate in animals, are caused by viruses, and are driven to emerge by ecological, behavioral, or socioeconomic changes. Acquired immunodeficiency syndrome (AIDS) of humans is caused by two lentiviruses, human immunodeficiency virus types 1 and 2 (HIV-1 and HIV-2). Here, we describe the origins and evolution of these viruses, and the circumstances that led to the AIDS pandemic. Both HIVs are the result of multiple cross-species transmissions of simian immunodeficiency viruses (SIVs) naturally infecting African primates [1]. In 2003, severe acute respiratory syndrome coronavirus (SARS-CoV) emerged and caused over 8,000 human cases of infection and more than 700 deaths worldwide. Zoonotic SARS-CoV likely evolved to infect humans by a series of transmission events between humans and animals for sale in China [2].

Humans can be infected with zoonotic influenza viruses, such as avian influenza virus subtype A(H5N1), A(H7N9), and A(H9N2) and swine influenza virus subtype A(H1N1), A(H1N2) and A(H3N2). Human infections are primarily acquired through direct contact with infected animals or contaminated environments, some these viruses have not acquired the ability of sustained transmission among humans. The primary concern surrounding the diseases is its ability to infect humans and their mutations. Simultaneous infection of humans by the zoonotic influenza viruses could theoretically generate novel...
influenza viruses with pandemic potential [3], [4], [5]. A pandemic caused by such a virus could become one of the worst in history because of the potential that the virus would be highly pathogenic such as H5N1 [6], [7].

Many epidemiology models have been developed for understanding the spread and control of the diseases. Various issues have been considered including the risk of the future pandemic among human populations. Most of the existing models, however, are based on the underlying assumption that the disease is already communicable among humans such as 1918 (Spanish) flu [8], [9], swine-origin influenza-A (H1N1) [10], [11] or 1957 Asian flu [12].

Studies based on molecular-biological and genomic analysis have been carried out to track possible virus mutation and recombination of the zoonotic influenza viruses [13], [14]. A virus mutation process could be in the form of antigenic shift or antigenic drift. Antigenic shift is the process by which two or more different strains of a virus combine to form a new subtype having a mixture of the surface antigens of the original strains. Antigenic drift describes small and gradual changes in the surface proteins (antigens) of the virus through random mutational processes [15], [16].

To the best of our knowledge, only a few published studies model the threat of an emerging pandemic due to H5N1 virus mutation by antigenic drift [17] or antigenic shift [18], [19] mechanisms. In animal-human cross-species virus transmission models, such as avian-human [18] and swine-human [20], a hypothetical mutant virus was viewed as a shift virus mutation of the virus. Later, a model that incorporates both drift and shift as evolution mechanisms of influenza was proposed in [19]. As in [13], the drift evolution of influenza was modeled by the total number of the amino-acid substitutions during the strain circulating time.

The exiting antigenic shift models assume that the avian influenza virus in a human is re-assorted and then mutated in “vivo” [18], [19]. The problem with these models is that there is no natural method for defining the mutation probability. It is assumed in this study that a pandemic threat is posed by a virus mutation as a result of recombination between a zoonotic influenza virus and a human influenza virus.

2. Material and methods

2.1 Assumptions

Human infection of a zoonotic virus (ZV) happens by means of direct virus transmission from infected animals to humans [21]. The existing models such as in [18],[19], consider one infected disease state only. In this study, the infected humans with ZV were classified as symptomatic and asymptomatic. This partition is important, since individuals in these groups are treated differently. Symptomatic individuals are very sick and are usually isolated while asymptomatic individuals are usually still active [22], [23].

It is assumed that only the asymptomatic individuals have the potential to host a virus mutation and that double virus co-infection happens only when an infected but asymptomatic human with ZV is subsequently infected by a human virus (HV). It was assumed that the virus re-combination of ZV and HV mutate in “vivo” into a new virus strain. The virus was referred to as a mutant virus (MV). It was assumed that the mutant virus can transmit between humans.

Thus, this study considers three influenza viruses that are spreading among linked populations of animals (or animals for short) and humans. The first virus is ZV. It is transmissible between animals, transmissible from animals to humans, but not between humans. The virus is highly virulent among animals and humans. The second virus is HV. It spreads and is communicable among humans but does not infect animals. It is not extremely virulent among humans. The third virus is the hypothetical MV described above. This virus is assumed to have the ability to spread among humans easily with much greater virulence and thus posing the threat of a pandemic.
2.2 The Model
Individuals in the interrelated population of animals and humans are assigned to seven compartments, each representing a specific disease state. Let \( Z(t) \) be the vector of disease state variables

\[
Z(t) = (X(t), Y(t), H(t), S(t), A(t), B(t), M(t))
\]

where \( X(t) \) is the proportion of susceptible animals, \( Y(t) \) is the proportion of infected animals with \( ZV \), \( H(t) \) is the proportion of susceptible humans, \( S(t) \) is the proportion of infectious humans with \( HV \), \( A(t) \) is the proportion of asymptomatic humans with \( ZV \), \( B(t) \) is the proportion of symptomatic humans with \( ZV \) and \( M(t) \) is the proportion of infectious humans with \( MV \). Each subpopulation is assumed to be homogeneous in the sense that its individuals have the same infectious periods, immunity periods and contact rates with individuals in other subpopulations.

Starting from an initial disease state \( Z(0) = Z_0 \), where \( Z_0 = (X_0, Y_0, H_0, S_0, A_0, B_0, M_0) \in \Omega \), the dynamic of the disease state \( Z(t) \in \Omega \) is described by an initial value problem

\[
\begin{align*}
\dot{X} &= \eta_x X - \delta_x X - \alpha_{yx} Y X \left(1 + \frac{K_{xh}}{S + \alpha_{xh} S}\right) + r_1 Y \\
\dot{Y} &= \alpha_{yx} Y X - \left(\delta_y + m_y + r_y\right) Y \\
\dot{H} &= \eta_h H - \delta_h H - \alpha_{yh} Y H - \alpha_a \kappa_{ah} S H - \alpha_{mb} \kappa_{mh} M H + r_S S \\
\dot{S} &= \alpha_a \kappa_{ah} S H - \left(\delta_h + m_a + r_a\right) S \\
\dot{A} &= \gamma_a \alpha_{ah} \kappa_{ah} Y H - \mu \alpha_a \kappa_{ah} S A - \left(\delta_h + m_a\right) A \\
\dot{B} &= \left(1 - \gamma_a\right) \alpha_{ah} \kappa_{ah} Y H - \left(\delta_h + m_a\right) B \\
\dot{M} &= \mu \alpha_a \kappa_{ah} S A + \alpha_{mb} \kappa_{mh} M H - \left(\delta_h + m_a\right) M \\
Z(0) &= Z_0, \quad Z_0 \in \Omega 
\end{align*}
\]

where \( \Omega \subseteq \mathbb{R}^7_+ \) is the set of all disease states,

\[
\Omega = \{Z(t) \mid 0 \leq t \leq \infty\}.
\]

The parameter space \( P \subseteq \mathbb{R}^{32} \),

\[
P = \{p = (p_j) : p_j = \eta_x, \eta_h, \delta_x, \delta_h, \alpha_{yx}, \alpha_{yh}, \alpha_{ah}, \alpha_{ah}, \mu, \alpha_a, \alpha_{mb}, \kappa_{ah}, \kappa_{ah}, \kappa_{ah}, \kappa_{ah}, \kappa_{ah}, \kappa_{ah}, m_x, m_y, m_a, m_m, r_y, r_a\}.
\]

\( \eta_x \) is the rate of animal offspring and restocking while \( \eta_h \) is the rate of human offspring and susceptible migration. \( \alpha_{yx} \) and \( \alpha_{yh} \) are \( ZV \) transmission rates from infectious animals to susceptible animal and humans, respectively. \( \kappa_{ah} \) and \( \kappa_{ah} \) are the number of effective contacts between infectious animals per-unit time with susceptible animals and humans, respectively. \( \alpha_{ah} \) and \( \alpha_{ah} \) are \( HV \) transmission rates from infectious human with \( HV \) to susceptible human and asymptomatic humans, respectively. \( \kappa_{ah} \) and \( \kappa_{ah} \) are the number of effective contacts between infectious humans with \( HV \) per-unit time with susceptible humans and asymptomatic humans, respectively. \( \delta_x \) and \( \delta_h \) are the death rates from natural incidences for animals and humans, respectively. \( \gamma_a \) is the probability of an infected human having no symptoms. \( m_x, m_y \) and \( m_a \) are \( ZV \) virulences among infectious animals, asymptomatic humans, and symptomatic humans, respectively. \( r_y \) and \( r_a \) are the recovery rates of infectious animals and humans, respectively. \( \mu \) is the probability of a recombination of \( ZV \) and \( HV \) resulting in a mutan-avian flu virus. \( \alpha_{mb} \) is the transmission...
rate of mutant-avian flu. It was proved in [24] that the dynamic system (1) (2) is a well behaved, i.e. having non-negative real solutions. It has six disease equilibria, they will be listed in Subsection 2.5.

2.3. Reproduction numbers
A reproduction number is the expected number of secondary infections produced in a completely susceptible population by a typical infected individual during entire period of infection [25], [26]. Let the state variable be reordered so that the first five elements of the new state variable correspond to infected subpopulations,

\[ Z = (Y, S, A, B, M, X, H). \]

In term of ordered variable \( Z \), (1) (2) can be written as

\[ \dot{Z} = f_1 + f_2 \]

where

\[
\begin{bmatrix}
\alpha_y \kappa_y YX \\
\alpha_s \kappa_s SH \\
\gamma_a \alpha_{sh} \kappa_{sh} YH - \mu \alpha_s \kappa_m SA \\
(1-\gamma_a) \alpha_{sh} \kappa_{sh} YH \\
\mu \alpha_s \kappa_m SA + \alpha_m \kappa_m MH \\
-\alpha_s \kappa_m MH - \alpha_{sh} \kappa_{sh} YX \\
-\alpha_{sh} \kappa_{sh} YH - \alpha_{sh} \kappa_{sh} SH - \alpha_m \kappa_m MH
\end{bmatrix},
\begin{bmatrix}
-\left(\delta_y + m_s + r_y\right)Y \\
-\left(\delta_h + m_s + r_y\right)S \\
-\left(\delta_h + m_s + r_h\right)A \\
-\left(\delta_h + m_s + r_m\right)M \\
\eta_s - \delta_s X + r_y Y \\
\eta_s - \delta_h H + r_s S
\end{bmatrix}.
\]

\[ \dot{Z}(0) = \bar{Z}_0, \bar{Z}_0 \in \Omega, \]

where \( \Omega \subseteq \mathbb{R}^7 \) is the set of all disease states,

\[ \Omega = \{Z(t)|0 \leq t \leq \infty\}. \]

The first part is the rates of new infection vector, while the second part is the rates of transfer vector due to births, deaths, disease mortalities and recoveries.

The dynamic system (3), (4) has a disease-free equilibrium

\[ Z^*_1 = (0,0,0,0,0,0,0). \]

At \( Z^*_1 \) the deriatives \( \Delta f_1(\bar{Z}^*_1) \) and \( \Delta f_2(\bar{Z}^*_1) \) can be partitioned as

\[ \Delta f_1(\bar{Z}^*_1) = \begin{bmatrix} F_1 & O \\ O & O \end{bmatrix}, \Delta f_2(\bar{Z}^*_1) = \begin{bmatrix} F_2 & O \\ J_3 & J_4 \end{bmatrix} \]

where
\[
F_1 = \begin{bmatrix}
\frac{\eta_h \alpha_{yh} \kappa_{yh}}{\delta_h} & 0 & 0 & 0 & 0 \\
0 & \frac{\eta_h \alpha_{sh} \kappa_{sh}}{\delta_h} & 0 & 0 & 0 \\
\gamma_a \alpha_{yh} \kappa_{yh} \eta_h \delta_h & 0 & 0 & 0 & 0 \\
(1-\gamma_a) \alpha_{yh} \kappa_{yh} \eta_h \delta_h & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & \frac{\eta_h \alpha_{mh} \kappa_{mh}}{\delta_h}
\end{bmatrix}
\]

and
\[
F_2 = \begin{bmatrix}
-\delta_y - m_y - r_y & 0 & 0 & 0 & 0 \\
0 & -\delta_h - m_y - r_y & 0 & 0 & 0 \\
0 & 0 & -\delta_h - m_a & 0 & 0 \\
0 & 0 & 0 & -\delta_h - m_b & 0 \\
0 & 0 & 0 & 0 & -\delta_h - m_m
\end{bmatrix}.
\]

\(F_1 \cdot F_2^{-1}\) is referred to as the next generation matrix. Here we compute the reproduction number as the spectral radius of the next generation matrix [25], [26]. The characteristic polynomials of the next generation matrix is given by
\[
X = w \left( w - \frac{\eta_h \alpha_{yh} \kappa_{yh}}{\delta_h (\delta_y + m_y + r_y)} \right) \left( w - \frac{\eta_h \alpha_{sh} \kappa_{sh}}{\delta_h (\delta_h + m_y + r_y)} \right) \left( w - \frac{\eta_h \alpha_{mh} \kappa_{mh}}{\delta_h (\delta_h + m_m)} \right).
\]

Therefore, the reproduction number for the ZV transmission among animals is given by
\[
R_{yx} = \frac{\eta_h \alpha_{yx} \kappa_{yx}}{\delta_y (\delta_y + m_y + r_y)}. \tag{5}
\]

The reproduction number for HV among humans is
\[
R_{nh} = \begin{cases} 
\frac{\eta_h \alpha_{sh} \kappa_{sh}}{\delta_h (\delta_h + m_y + r_y)} & \text{if } R_{yx} \leq 1 \\
1 - \left(1 - \frac{1}{R_{yx}}\right) R_{jh} & \text{if } R_{yx} > 1, R_{jh} > 1,
\end{cases} \tag{6}
\]

where
\[
R_{jh} = \frac{\eta_h \alpha_{yh} \kappa_{yh}}{\delta_h (\delta_y + m_y + r_y)}. \tag{7}
\]

The reproduction number for ZV transmission to the infected human who is asymptomatic is
The reproduction number for MV among humans is

\[ R_{mh} = \begin{cases} \frac{\eta_h \alpha_{mh} \kappa_{mh}}{\delta_h (\delta_h + m_h)} & \text{if } R_{yx} \leq 1 \\ 1 - \frac{1}{(1 - \frac{1}{R_{xy}}) R_{yh}} & \text{if } R_{yx} > 1, R_{yh} > 1, \end{cases} \]  

The reproduction numbers are functions estimated from epidemic parameters for which their actual values are not known precisely. Hence, the effects of parameter uncertainties on the predictions of reproduction numbers should be addressed. This can be accomplished by sensitivity and uncertainty analysis using the proposed ranges of the reproduction parameters. Such analysis can be used for various purposes, such as ranking the parameters in order of their relative importance to the results and for assessing changes in the results due to variability in the parameter ranges. This is particularly important in studying the reproduction numbers whose behavior may only be understood by numerical analysis. The analysis of reproduction numbers is carried out by a simple method proposed in [27],[28]. Consider first the reproduction number for ZV transmission among animals.

\[ A_p = \frac{p}{R_{yx}} \frac{\partial R_{yx}}{\partial p} \begin{cases} = 1 & \text{if } p = \eta_x, \alpha_{xy}, \kappa_{yx} \\ < 1 & \text{if } p = \delta_h, m_h, r_y. \end{cases} \]

Since \( \eta_x \) is fixed, \( R_{yx} \) is most sensitive to the change of \( \alpha_{xy}, \kappa_{yx} \). Similarly, \( R_{yh} \) is most sensitive to the change of \( \alpha_{yh}, \kappa_{yh} \). \( R_{sh} \) is most sensitive to the change of \( \alpha_{sh}, \kappa_{sh} \). \( R_{mh} \) is most sensitive to the change of \( \alpha_{mh}, \kappa_{mh} \).

2.5. Disease state equilibria

Other then the disease-free equilibrium

\[ Z_1 = (\eta_x, 0, \eta_h, 0, 0, 0, 0), \]

the disease dynamic (1) (2) has five more disease state equilibria. The second is HV epidemic equilibrium

\[ Z_2 = (X^*_1, 0, H^*_2, S^*_2, 0, 0, 0, 0), \]

where \( H_2^* = \frac{\eta_h}{\delta_h} \frac{1}{R_{sh}} \) and \( S_2^* = \frac{\eta_h}{\delta_h + m_h} (1 - \frac{1}{R_{sh}}) \). The third disease state equilibrium is the state in which there are no animals or humans infected by the ZV and no humans infected by HV but there are humans infected by MV,

\[ Z_3 = (X^*_1, 0, H^*_2, 0, 0, 0, M^*_3), \]

where \( H_3^* = \frac{\eta_h}{\delta_h} \frac{1}{R_{sh}} \) and \( M_3^* = \frac{\eta_h}{\delta_h + m_h} (1 - \frac{1}{R_{mh}}) \). The fourth, the human epidemic equilibrium state, is

\[ Z_4 = (X^*_1, 0, H^*_4, S^*_4, A^*_4, 0, M^*_4), \]
The sixth avian flu is epidemic among humans, 

Theorem 1. and full proofs are available elsewhere [24]. as asymptotically stable (GAS) of the six disease equilibria. Outlines of the proofs are given in the appendices, where 

The fifth equilibrium state corresponds to the fifth equilibrium state corresponds to where 

Theorem 2. Proof. 

2.6 Stability analysis 

The following theorems provide statements regarding the local asymptotically stable (LAS) and global asymptotically stable (GAS) of the six disease equilibria. Outlines of the proofs are given in the appendices, and full proofs are available elsewhere [24].

**Theorem 1.** If \( R_{yh} \leq 1, R_{sh} \leq 1, R_{mh} \leq 1, R_{sh} \leq 1 \) then \( Z_v^* = (X_v^*, 0, H_v^*, 0, 0, 0, 0) \) is GAS on \( \Omega_1 \), where \( \Omega_1 = \{ Z = (X, Y, H, S, A, B, M) : X \geq 0, Y \geq 0, H \geq 0, S \geq 0, A \geq 0, B \geq 0, M \geq 0 \} \).

**Proof.** See Appendix A.

**Theorem 2.** If \( R_{yh} \leq 1, R_{sh} \geq 1, R_{mh} \leq 1, R_{sh} \leq 1 \) then \( Z_v^* \) is GAS on \( \Omega_2 \), where

\( \Omega_2 = \{ Z = (X, Y, H, S, A, B, M) : X > 0, Y \geq 0, H > 0, S > 0, A \geq 0, B \geq 0, M \geq 0 \} \).

**Proof.** See Appendix B.

**Theorem 3.** If \( R_{yh} \leq 1, R_{sh} \leq 1, R_{mh} > 1, R_{sh} \leq 1 \) then \( Z_v^* \) is GAS on \( \Omega_3 \), where
\[ \Omega_3 = \{Z = (X, Y, H, S, A, B, M) : X > 0, Y \geq 0, H > 0, S > 0, A \geq 0, B \geq 0, M > 0\}. \]

**Proof.** See Appendix C.

**Theorem 4.** If \( R_{yx} \leq 1, R_{sh} \leq 1, R_{mh} > 1, R_{aw} \leq 1 \) then \( Z^*_4 \) is GAS on \( \Omega_4 \), where
\[ \Omega_4 = \{Z = (X, Y, H, S, A, B, M) : X > 0, Y \geq 0, H > 0, S > 0, A > 0, B \geq 0, M > 0\}. \]

**Proof.** See Appendix D.

**Theorem 5.** If \( R_{yx} > 1, R_{sh} \leq 1, R_{mh} \leq 1, R_{aw} \leq 1 \), then \( Z^*_5 \) is LAS.

**Proof.** See Appendix E.

**Theorem 6.** If \( R_{yx} > 1, R_{sh} \leq 1, R_{mh} > 1, R_{aw} > 1 \) then \( Z^*_6 \) is LAS.

**Proof.** See Appendix F.

### 3. Discussion and conclusion

Theorem 1 shows that all diseases will be eliminated if only if the following conditions are satisfied

\[ \kappa_{yx} \leq \frac{\delta_x (\delta_x + m_y + r_y)}{\eta_x \alpha_{yx}}, \quad (10) \]

\[ \kappa_{yh} \leq \frac{\delta_h}{\eta_h \alpha_{yh}} (\delta_y + m_y), \quad (11) \]

\[ \kappa_{aw} \leq \frac{\delta_a}{\eta_a \alpha_{aw}} (\delta_a + m_a + m_y) \quad (12) \]

and

\[ \kappa_{mh} \leq \frac{\delta_m}{\eta_m \alpha_{mh}} (\delta_h + m_m) \quad (13) \]

Theorem 2 shows that if conditions (10) (12) and (13) are satisfied but condition (11) is not satisfied then there will be no disease except MV. Theorem 3 shows that if conditions (10) (11) and (13) are satisfied but condition (12) is not satisfied then there will be no disease except HV. Theorem 4 shows that if the conditions (10) (11) and (13) are satisfied but condition (12) is not satisfied then there are humans who have HV and have ZV but are asymptomatic for ZV and who have HV, ZV and MV but are asymptomatic for ZV. Theorems 1 to 4 are satisfied when there is no epidemic among animals while Theorems 5 to 6 are satisfied when there is an epidemic among animals. Theorem 5 and Theorem 6 show that when \( R_{yx} > 1 \) and there is epidemic among animals, then there will be a ZV outbreak among humans. In addition to the condition \( R_{yx} > 1 \), if \( R_{mh} > R_{sh} \), then there will be outbreaks of ZV and MV among humans. It can be concluded that; (i) to control the spread of disease means to control the effective rate of disease transmissions, (ii) containing ZV in the animal world does not stop the spread of the implicated diseases in the human world, (iii) the spread of mutant-avian-flu has a bigger magnitude than ZV in terms of the proportion of individuals acquiring the disease, (iv) reducing the contact among animals will reduce the spread of ZV but not HV and mutant-avian-flu, (v) social distancing programs reduce the number human casualties.
Appendices

Appendix A: Proof for Theorem 1

Proof. The characteristic polynomial of the Jacobian matrix of the disease dynamic (1),(2) evaluated at $Z_1$ is
\[
X_1 = w[w + \delta_x][w + (\delta_h + m_y)][w + (\delta_h + m_y)(1 - R_{sh})] \\
\times [w + (\delta_h + m_y + r_y)(1 - R_{sh})][w + (\delta_h + m_y)(1 - R_{mh})] = 0
\]
The first eigenvalue is zero. Since parameter values $\delta_x, \delta_h, r_y, m_y, m_x, m_h, m_b$ are all positive numbers, the $2^{nd}, 3^{rd}, 4^{th}$ eigenvalues are negative real numbers. Since $R_{sh} \leq 1$ then $5^{th}$ eigenvalue $-(\delta_h + 2m_y)(1 - R_{sh})$ is negative. Since $R_{xy} \leq 1$, the $6^{th}$ eigenvalue $-(\delta_h + m_y + r_y)(1 - R_{sh})$ is negative. Since $R_{mh} \leq 1$ then the $7^{th}$ eigenvalue $-(\delta_h + m_y)(1 - R_{mh})$ is negative. Since all eigenvalues are negative real numbers, the Jacobian matrix is locally stable at DFE $Z_1^*$. It is easy to show that all minors of the Jacobian matrix are also stable at DFE $Z_1^*$. Since the Jacobian matrix and its minors are stable at $Z_1^*$, $Z_1^*$ is LAS.

Consider the third equation of (1). Since the disease transmissions reduce the number of healthy humans $\dot{H} \leq \eta_h - \delta_h H$. Integrating the inequality over $[0, t]$ results in $H(t) \leq H_0^* + |H(0) - H_1^*| e^{-\delta_h t}$. Therefore $\forall \varepsilon > 0, \exists t_1$ such that $1 |H(0) - H_1^*| e^{-\delta_h t} \leq \varepsilon$ for any $t > t_1$.

Hence $H(t) \leq H_1^* + \varepsilon$ for $t \geq t_1$. Thus for $T_1 \geq t_1, \limsup_{t \to T_1} H(t) \leq H_1^* + \varepsilon$. Letting $T_1 \to \infty$, results in $H^\infty \leq H_1^* + \varepsilon$, $H^\infty \leq H_1^*$ for $\varepsilon > 0$. Therefore, for any initial disease state $Z(0)$ there will always exist $\omega(Z(0))$, the $\omega$-limit set of orbit through $Z(0)$.

Since $Z_1^*$ is LAS and $\lim_{t \to \infty} X(t) = \frac{\eta_x}{\delta_x} = X(0)$ and $\lim_{t \to \infty} Y(t) = 0$ whenever $R_{xy} \leq 1$.

Having $Y = 0$ in the equation number 6 of (1) and integrating it over $[0, \infty)$ results in $\lim_{t \to \infty} B(t) = 0$. For any initial disease state $Z(0)$ there will always exist $\omega(Z(0))$, $\omega$-limit set of orbit through $Z(0)$ in $G_1$, where $G_1 = \{Z = (X, Y, H, S, A, B, M) : X > 0, Y = 0, H > 0, S = 0, A = 0, B = 0, M = 0\}$. Therefore, $Z_1^*$ is GAS on $G_1$. Since $Z_1^*$ is LAS on $\Omega_1$ then by the Poincare-Bendixon theorem [12] $Z_1^*$ is GAS on $\Omega_1$.

Appendix B: Proof for Theorem 2

Proof. The characteristic polynomial of the Jacobian matrix of the disease dynamic (1),(2) evaluated at $Z_2$ is
\[
X_2 = w[w + \delta_x][w + (\delta_h + m_y)][w + (\delta_h + m_y)(1 - R_{sh})] \\
\times [w + (\delta_h + m_y + r_y)(1 - R_{sh})][w + (\delta_h + m_y)(1 - R_{mh})] = 0
\]
The non-zero eigen values are negative real numbers. Therefore, the Jacobian matrix and its all minors are stable at $Z_2^*$, therefore $Z_2^*$ is LAS. Similar to the previous proof, for any initial disease
state $Z(0)$ there will always exist $\omega(Z(0))$, $\omega$-limit set of orbit through $Z(0)$ in $G_2$ for $G_2 = \{Z = (X, Y, H, S, A, B, M) : X > 0, Y = 0, H \geq 0, S > 0, A = 0, B = 0, M = 0\}$. Therefore, $Z^*_2$ is GAS on $G_2$. Since $Z^*_2$ is LAS on $\Omega_2$ then $Z^*_2$ is GAS on $\Omega_2$.

**Appendix C:** Proof for Theorem 3

*Proof.* At $Z_3$, the characteristic polynomial of the Jacobian matrix of the disease dynamic (1), (2) is

$$X_3 = w^3\left[w + \delta_h + m_y \right]\left[w + (\delta_h + m_y)\right]\left[w + \delta_h + m_y + r_y \right](1 - R_{sh}) = 0$$

The non-zero eigen values are negative real numbers. The Jacobian matrix and its all minors are stable at $Z^*_3$, therefore $Z^*_3$ is LAS. $Z^*_3$ is GAS on $G_3$ for $G_3 = \{Z = (X, Y, H, S, A, B, M) : X > 0, Y = 0, H \geq 0, S = 0, A = 0, B = 0, M > 0\}$. Since $Z^*_3$ is also LAS on $\Omega_3$ then $Z^*_3$ is GAS on $\Omega_3$.

**Appendix D:** Proof for Theorem 4

*Proof.* The characteristic polynomial of the Jacobian matrix of the disease dynamic (1), (2) evaluated at $Z_4$ is

$$X_4 = w^3\left[w + (\delta_h + m_y)\right]\left[w + 2(\delta_h + m_y)\right]\left[w + (\delta_h + m_y + r_y)\right](r_0 - 1) = 0$$

The non-zero eigen values are negative real numbers. The Jacobian matrix and its all minors are stable at $Z^*_4$, therefore $Z^*_4$ is LAS. $Z^*_4$ is GAS on $G_4$ for $G_4 = \{Z = (X, Y, H, S, A, B, M) : X > 0, Y = 0, H \geq 0, S > 0, A > 0, B = 0, M > 0\}$. Since $Z^*_4$ is also LAS on $\Omega_4$ then $Z^*_4$ is GAS on $\Omega_4$.

**Appendix E:** Proof for Theorem 5

*Proof.* At $Z_5$, the eigen values of the characteristic polynomial of the Jacobian matrix of the disease dynamic (1), (2) is

$$X_5 = w^3\left[w + \frac{-\alpha_{mh}K_{mh}\delta_h - \alpha_{mh}K_{mh}m_y - \alpha_{mh}K_{mh}r_y + \delta_h\alpha_{mh}K_{mh}m_y + m_y\alpha_{mh}K_{mh}}{\alpha_{mh}K_{mh}}\right]\left[w + 1/2\frac{\alpha_{xy}\kappa_{xy}m_y - r_y + \sqrt{Q1}}{\delta_x + m_y}\right]\left[w + 1/2\frac{\alpha_{xy}\kappa_{xy}m_y - r_y\delta_x + \sqrt{Q2}}{\delta_x + m_y}\right] = 0$$

where

$$Q1 = \alpha_{xy}\kappa_{xy}m_y^2 - 2\alpha_{xy}\kappa_{xy}m_yr_y\delta_y + r_y^2\delta_y^2 + 8\delta_y\kappa_{xy}m_y^2 - 8\delta_y\kappa_{xy}m_y\delta_y^2 + 4\kappa_{xy}m_y^2\delta_y^3 + 12\delta_y^3m_y + 12m_y^2\delta_y^2 + 4\kappa_{xy}m_y^2 + 4m_y^3\delta_y$$

and
\[ Q2 = \alpha_{yx}^2 \kappa_{yx}^2 n_x^2 - 2 \alpha_{yx} \kappa_{yx} \eta_x r_1 \delta_1 + r_2 \delta_1^2 + 8 r_1 \delta_1 m_y^2 - 8 \delta_1 \alpha_{yx} \kappa_{yx} \eta_x m_y - 4 \alpha_{yx} \kappa_{yx} \eta_x \delta_1^2 + 4 r_1 \delta_3^1 + 12 \delta_3^3 m_y \\
+ 12 m_y^3 \delta_1 + 4 \delta_4^4 + 4 r_1 \delta_1 m_y^2 - 4 \alpha_{yx} \kappa_{yx} \eta_x m_y^2 + 4 m_3^m \delta_x, \]

The non-zero eigen values are negative real numbers. The Jacobian matrix and its all minors are stable at \( Z_s^* \), therefore \( Z_s^* \) is LAS.

**Appendix F: Proof for Theorem 6**

*Proof.* At \( Z_s \) the characteristic polynomial of the Jacobian matrix of the disease dynamic (1),(2) is

\[
X_0 = w^3 \left[ w - \frac{-\alpha_{mh} \kappa_{mh} \delta_h - \alpha_{mh} \kappa_{mh} m_1 - \alpha_{mh} \kappa_{mh} r_1 + \delta_h \alpha_{mh} \kappa_{mh} + m_2 \alpha_{mh} \kappa_{mh} \delta_h}{\alpha_{mh} \kappa_{mh} \delta_h} \right] \\
\times \left[ w + \frac{\alpha_{yx} \kappa_{yx} \eta_x - r_1 \delta_1 \sqrt{Q1}}{\delta_x + m_y} \right] \left[ w + \frac{\alpha_{yx} \kappa_{yx} \eta_x - r_1 \delta_1 \sqrt{Q2}}{\delta_x + m_y} \right] \\
\times \left[ w - \delta_h - m_1 \right] \left[ w - \delta_h - m_2 \right],
\]

where

\[ Q1 = \alpha_{yx}^2 \kappa_{yx}^2 \eta_x^2 - 2 \alpha_{yx} \kappa_{yx} \eta_x r_1 \delta_1 + \delta_1 \delta_1^2 + 8 \delta_1 \alpha_{yx} \kappa_{yx} \eta_x m_1 - 8 \delta_1 \alpha_{yx} \kappa_{yx} \eta_x m_1 + 4 r_1 \delta_3^1 - 4 \alpha_{yx} \kappa_{yx} \eta_x \delta_1^2 \\
+ 12 \delta_3^3 m_1 + 12 m_1^3 \delta_1 + 4 \delta_4^4 + 4 r_1 \delta_1 m_1^2 - 4 \alpha_{yx} \kappa_{yx} \eta_x m_1^2 + 4 m_3^m \delta_x \]

and

\[ Q2 = \alpha_{yx}^2 \kappa_{yx}^2 n_x^2 - 2 \alpha_{yx} \kappa_{yx} \eta_x r_1 \delta_1 + r_2 \delta_1^2 + 8 r_1 \delta_1 m_y^2 - 8 \delta_1 \alpha_{yx} \kappa_{yx} \eta_x m_y + 4 r_1 \delta_3^1 + 12 \delta_3^3 m_y \\
- 4 \alpha_{yx} \kappa_{yx} \eta_x \delta_1^2 + 12 m_y^3 \delta_1 + 4 \delta_4^4 + 4 r_1 \delta_1 m_y^2 - 4 \alpha_{yx} \kappa_{yx} \eta_x m_y^2 + 4 m_3^m \delta_x. \]

The non-zero eigen values are negative real numbers. The Jacobian matrix and its all minors are stable at \( Z_s^* \), therefore \( Z_s^* \) is LAS.

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