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QUALITATIVE ANALYSIS OF AN AGE- AND SEX-STRUCTURED VACCINATION MODEL FOR HUMAN PAPILLOMAVIRUS

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Abstract. A new model for the transmission dynamics of human pappilomavirus (HPV) is designed and analysed. The model, which stratifies the total population in terms of age and gender, incorporates an imperfect anti-HPV vaccine with some therapeutic benefits. Rigorous qualitative analysis of the resulting age-structured model, which takes the form of a deterministic system of non-linear partial differential equations with separable transmission coefficients, shows that the disease-free equilibrium of the model is locally-asymptotically stable whenever the effective reproduction number (denoted by $\mathcal{R}_v$) is less than unity. It is shown to be globally-asymptotically stable if certain additional conditions hold. Furthermore, it is shown that the model has at least one endemic equilibrium when $\mathcal{R}_v$ exceeds unity. Hence, the effective control of HPV spread in a community, using a vaccine, is governed by the threshold quantity $\mathcal{R}_v$ (the use of the vaccine will lead to effective disease control or elimination only if it reduces the threshold quantity to a value less than unity; and the use of such vaccine will not lead to effective disease control if it fails to make the threshold quantity to be less than unity).

1. **Introduction.** The human papillomavirus (HPV) accounts for most of the commonly-occurring viral infections among sexually-active people [10]. Over 100 types have been molecularly characterized to date, and about 40 types have been found in the genital tract of men and women [10]. The spectrum of HPV-associated diseases is broad and significant. Persistent infection with high-risk HPV is causally

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linked to cancers of the cervix, vulva, vagina, penis, anus, oral cavity, and oropharynx [4, 25]. The total HPV infection-attributable cancers in 2002 is estimated at 561,100, with majority of the burden being in developing countries [24]. Prominent among these cancers is cervical cancer, which is considered to be the second most common malignancy among women (and a leading cause of cancer death worldwide) [10]. The persistence of HPV infection is a significant risk factor for recurrence [6]. The low-risk HPV types 6 and 11 cause ano-genital warts and recurrent respiratory papillomatosis, with both conditions resulting in substantial healthcare costs [10, 19].

A quadrivalent HPV (Types 6, 11, 16, 18) and a bivalent (Types 16, 18) recombinant vaccines have been approved for use worldwide. Prophylactic HPV vaccines can be effective in controlling the spread of HPV and the diseases related to it [10]. The efficacy of the prophylactic quadrivalent HPV vaccines is 90% [28] and that of the prophylactic bivalent vaccine ranges from 91.6% to 100% (100% efficacy against persistent infections). Although the age range of the populations targeted is similar, there are major differences in the use of these vaccines by gender. For example, while both vaccines are recommended to girls and women age 12–26 years, only the quadrivalent vaccine is recommended for boys and men [10].

Several mathematical models have been constructed to assess the epidemiological consequences and cost effectiveness of prophylactic HPV vaccination strategies. Because the risk of HPV infection differs by age and gender, various studies of the cost effectiveness of vaccination strategies based on sex and age have been carried out [5, 8, 18, 23]. For example, the assessment of the extension of vaccination to males of ages 9 – 26 shows a decrease in the cumulative mean number of genital wart cases, cervical intraepithelial neoplasia 2/3 cases, cancer cases, and cancer deaths in a population [11]. The vast majority of models for HPV transmission with an imperfect vaccine are of the form of systems of ordinary differential equations (ODEs) [2, 9, 10, 15]. In a recent study, Al-Arydah and Smith? [1] have formulated the above scenario in the form of an age-structured, two-sex model based on a system of partial differential equations, which incorporates an HPV vaccine administered to females only. The analyses focus on the comparison of the impact of vaccination in childhood and adult stages and it is shown that mass vaccination of a single age cohort in one gender may result in the control of HPV across all age groups. Furthermore, the above cited modelling studies (with the exception of [10]) do not include persistent HPV infection.

The aim of this study is to design and rigorously analyse a more realistic HPV vaccine model that takes into account variabilities in gender and age. In other words, a new two-sex age-structured model will be designed and used to assess the community-wide impact of an imperfect HPV vaccine.

2. **Model formulation.**

The model, which incorporates an imperfect HPV vaccine, considers the dynamics of the total male and female populations (characterized by the subscripts m and f, respectively). The total male population, denoted by $N_m(a,t)$ at time t and age a ($0 \leq a < \sigma$, where σ denotes the highest age attained by individuals in the population), is divided into seven mutually-exclusive compartments, namely susceptible males ($S_m(a,t)$), vaccinated males ($V_m(a,t)$), unvaccinated infectious males ($I_m(a,t)$), vaccinated infectious males ($I_{mv}(a,t)$), unvaccinated males with persistent infection ($P_m(a,t)$), vaccinated males with persistent infection ($P_{mv}(a,t)$), and recovered male individuals ($R_m(a,t)$). The total female population of age a at time t, denoted by $N_f(a,t)$, is similarly divided into seven mutually-exclusive compartments, namely susceptible females ($S_f(a,t)$), vaccinated females ($V_f(a,t)$), unvaccinated infectious females ($I_f(a,t)$), vaccinated infectious females ($I_{fv}(a,t)$), unvaccinated females with persistent infection ($P_f(a,t)$), vaccinated females with persistent infection ($P_{fv}(a,t)$) and recovered female individuals ($R_f(a,t)$), so that

$$\begin{aligned} N_m(a,t) &= S_m(a,t) + V_m(a,t) + I_m(a,t) + P_m(a,t) + I_{mv}(a,t) \\ &\quad + P_{mv}(a,t) + R_m(a,t), \\ N_f(a,t) &= S_f(a,t) + V_f(a,t) + I_f(a,t) + P_f(a,t) + I_{fv}(a,t) + P_{fv}(a,t) + R_f(a,t). \end{aligned}$$

It is assumed that the total population (of males and females) is in a stationary demographic state, with the total male and female population (for $j = m, f$) given, respectively, by [13, 16]

$$\mathcal{N}_j(a) := N_j(a,\infty) = \mu^* N_{j0} \exp\left(-\int_0^a \mu(\xi)d\xi\right), \tag{1}$$

with,

$$\mu^* \int_0^\sigma \exp\left(-\int_0^a \mu(\xi)d\xi\right) da = 1,$$

where μ^* is the *per* capita birth rate [13], N_{m0} and N_{f0} are the initial population sizes of males and females respectively, and $\mu(a)$ is the age-dependent natural death rate. Following [16], it is assumed that $\mu(a)$ is non-negative, locally-integrable on $[0,\sigma)$ and satisfies

$$\int_0^\sigma \mu(\xi)d\xi = \infty.$$

The term $\exp\left(-\int_0^a \mu(\xi)d\xi\right)$ represents the survival function (i.e., the proportion of individuals who survive to age a). It should be noted that $\mathcal{N}_j(\sigma) = 0$, for $j \in \{m, f\}$.

The model for the transmission dynamics of HPV, in the presence of an imperfect anti-HPV vaccine, is given by the following age-structured system of non-linear partial differential equations (PDEs):

$$\begin{aligned} \left(\frac{\partial}{\partial a} + \frac{\partial}{\partial t}\right) S_m(a,t) &= -\lambda_m(a,t)S_m(a,t) + \omega_m V_m(a,t) - \psi_m(a)S_m(a,t) \\ &\quad - \mu(a)S_m(a,t), \\ \left(\frac{\partial}{\partial a} + \frac{\partial}{\partial t}\right) V_m(a,t) &= \psi_m(a)S_m(a,t) - \omega_m V_m(a,t) - \theta_{mv}\lambda_m(a,t)V_m(a,t) \\ &\quad - \mu(a)V_m(a,t), \\ \left(\frac{\partial}{\partial a} + \frac{\partial}{\partial t}\right) I_m(a,t) &= \lambda_m(a,t)S_m(a,t) - \rho_m I_m(a,t) - \mu(a)I_m(a,t), \\ \left(\frac{\partial}{\partial a} + \frac{\partial}{\partial t}\right) P_m(a,t) &= q_1\rho_m I_m(a,t) - \kappa_m P_m(a,t) - \mu(a)P_m(a,t), \\ \left(\frac{\partial}{\partial a} + \frac{\partial}{\partial t}\right) I_{mv}(a,t) &= \theta_{mv}\lambda_m(a,t)V_m(a,t) - \rho_{mv} I_{mv}(a,t) - \mu(a)I_{mv}(a,t), \end{aligned}$$

$$\begin{aligned}
\left(\frac{\partial}{\partial a}+\frac{\partial}{\partial t}\right)P_{mv}(a,t) &= q_2\rho_{mv}I_{mv}(a,t)-\kappa_{mv}P_{mv}(a,t)-\mu(a)P_{mv}(a,t),\\
\left(\frac{\partial}{\partial a}+\frac{\partial}{\partial t}\right)R_m(a,t) &= (1-q_1)\rho_m I_m(a,t)+\kappa_m P_m(a,t)\\
&\quad +(1-q_2)\rho_{mv}I_{mv}(a,t)+\kappa_{mv}P_{mv}(a,t)-\mu(a)R_m(a,t),\\
\left(\frac{\partial}{\partial a}+\frac{\partial}{\partial t}\right)S_f(a,t) &= -\lambda_f(a,t)S_f(a,t)+\omega_f V_f(a,t)-\psi_f(a)S_f(a,t)\\
&\quad -\mu(a)S_f(a,t),\\
\left(\frac{\partial}{\partial a}+\frac{\partial}{\partial t}\right)V_f(a,t) &= \psi_f(a)S_f(a,t)-\omega_f V_f(a,t)-\theta_{fv}\lambda_f(a,t)V_f(a,t)\\
&\quad -\mu(a)V_f(a,t),\\
\left(\frac{\partial}{\partial a}+\frac{\partial}{\partial t}\right)I_f(a,t) &= \lambda_f(a,t)S_f(a,t)-\rho_f I_f(a,t)-\mu(a)I_f(a,t),\\
\left(\frac{\partial}{\partial a}+\frac{\partial}{\partial t}\right)P_f(a,t) &= p_1\rho_f I_f(a,t)-\kappa_f P_f(a,t)-\mu(a)P_f(a,t),\\
\left(\frac{\partial}{\partial a}+\frac{\partial}{\partial t}\right)I_{fv}(a,t) &= \theta_{fv}\lambda_f(a,t)V_f(a,t)-\rho_{fv}I_{fv}(a,t)-\mu(a)I_{fv}(a,t),\\
\left(\frac{\partial}{\partial a}+\frac{\partial}{\partial t}\right)P_{fv}(a,t) &= p_2\rho_{fv}I_{fv}(a,t)-\kappa_{fv}P_{fv}(a,t)-\mu(a)P_{fv}(a,t),\\
\left(\frac{\partial}{\partial a}+\frac{\partial}{\partial t}\right)R_f(a,t) &= (1-p_1)\rho_f I_f(a,t)+\kappa_f P_f(a,t)+(1-p_2)\rho_{fv}I_{fv}(a,t)\\
&\quad +\kappa_{fv}P_{fv}(a,t)-\mu(a)R_f(a,t).
\end{aligned} \tag{2}$$

In (2), $\lambda_m(a,t)$ is the rate at which unvaccinated susceptible males acquire HPV infection from infected females (force of infection), and is given by (see also [9]):

$$\lambda_m(a,t)=\int_0^\sigma \mathcal{B}_m(a,b)\left[\frac{I_f(b,t)+\eta_{1f}P_f(b,t)+\eta_{2f}I_{fv}(b,t)+\eta_{3f}P_{fv}(b,t)}{\mathcal{N}_f(b)}\right]db, \tag{3}$$

where $\mathcal{B}_m(a,b)$ is the effective contact rate of males of age a with females of age b ($0\le b<\sigma$). Furthermore, $0\le \eta_{1f},\ \eta_{2f},\ \eta_{3f}\le 1$ are the modification parameters accounting for the relative infectiousness of individuals in the P_f, I_{fv} and P_{fv} classes, in comparison to those in the I_f class, respectively. The contact rate ($\mathcal{B}_m(a,b)$) is an aggregate parameter defined as $\mathcal{B}_m(a,b)=c_m(a,b)\beta_m(a,b)$, where $c_m(a,b)$ is the average number of female partners of age b for a male of age a, and $\beta_m(a,b)$ is the probability of HPV transmission, from an infected female of age b to a susceptible male of age a, *per* contact [9]. The rate $\mathcal{B}_f(a,b)=c_f(a,b)\beta_f(a,b)$ is similarly defined. Furthermore, the following conservation law (for number of sexual contacts made by males balancing those made by females) [9] is assumed to hold:

$$c_m(a,b)\mathcal{N}_m(a)=c_f(b,a)\mathcal{N}_f(b). \tag{4}$$

A solution to (4) is given by

$$c_m(a,b)=CN_f(b) \text{ and } c_f(b,a)=CN_m(a), \tag{5}$$

where C is the average number of sexual contacts made between males of age a and females of age b, *per* unit time. Using (5), the force of infection, (3), can now be re-written as:

$$\lambda_m(a,t) = C\int_0^\sigma \beta_m(a,b)\left[I_f(b,t)+\eta_{1f}P_f(b,t)+\eta_{2f}I_{fv}(b,t)+\eta_{3f}P_{fv}(b,t)\right]db.$$

Unvaccinated susceptible males are vaccinated at an age-dependent rate $\psi_m(a)$. Vaccinated susceptible males acquire breakthrough infection at a reduced rate $\theta_{mv}\lambda_m(a,t)$, where $1-\theta_{mv}$ (with $0 \le \theta_{mv} < 1$) represents the vaccine efficacy in preventing breakthrough infection, and lose their vaccine-acquired immunity (and return to the class of unvaccinated susceptible males) at a rate ω_m. Individuals in all epidemiological classes suffer natural death at an age-dependent rate $\mu(a)$. The population of unvaccinated infectious individuals (I_m) is generated at the rate $\lambda_m(a,t)$. Individuals in this class leave at a rate ρ_m (a fraction, q_1, of these individuals move to the class of individuals with persistent HPV infection, P_m; while the remaining fraction, $1-q_1$, move to the class of recovered individuals, R). It should be mentioned that the model (2) does not allow for disease-induced death. It is worth emphasizing that the aforementioned phenomenon of persistent infection, a notable feature of HPV disease [6, 12, 25, 27], is often overlooked in HPV modeling studies. Individuals in the I_m (P_{mv}) class recover at a rate κ_m (κ_{mv}). Infectious vaccinated individuals (in the I_{mv} class) leave this class at a rate ρ_{mv} (a fraction, q_2, of these individuals develop persistent infection (and move to the P_{mv} class; while the remaining fraction, $1-q_2$, move to the recovered class, R).

Unvaccinated and vaccinated susceptible females acquire HPV infection at the rates

$$\lambda_f(a,t) = C\int_0^\sigma \beta_f(a,b)\left[I_m(b,t)+\eta_{1m}P_m(b,t)+\eta_{2m}I_{mv}(b,t)+\eta_{3m}P_{mv}(b,t)\right]db,$$

and $\theta_{fv}\lambda_f(a,t)$ respectively, where $1-\theta_{fv}$ (with $0 \le \theta_{fv} < 1$) represents the vaccine efficacy in preventing breakthrough infection in females. The parameters associated with the equations for the female compartments ($S_f, V_f, I_f, P_f, I_{fv}$ and P_{fv}) in the model (2) are defined in the same way as the corresponding parameters for the male compartments defined above. A schematic description of the model is given in Figure 1 (the associated variables and parameters of the model are described in Tables 1 and 2, respectively).

It is assumed that all individuals are born susceptible and unvaccinated (at $a = 0$). Thus,

$$\begin{aligned} S_j(0,t) = \mu^* N_{j0},\ V_j(0,t) &= I_j(0,t) = P_j(0,t) = I_{jv}(0,t) \\ &= P_{jv}(0,t) = R_j(0,t) = 0,\ j \in \{m,f\}. \end{aligned} \tag{6}$$

The initial values of the variables of the model (2) are given by:

$$\begin{aligned} &S_j(a,0) = S_{j0}(a), V_j(a,0) = V_{j0}(a), I_j(a,0) = I_{j0}(a), P_j(a,0) = P_{j0}(a), \\ &I_{jv}(a,0) = I_{jv0}(a), P_{jv}(a,0) = P_{jv0}(a), R_j(a,0) = R_{j0}(a),\ j \in \{m,f\}. \end{aligned} \tag{7}$$

The model (2) is the extension of the SIR ODE model with vaccination given in [9], by adding the effect of age-structure, vaccine-induced immunity and persistent infection. It also extends the agent-based model in [10] (which also includes waning vaccine immunity, persistent infections and 17 age groups) by treating age as a continuous variable. The model (2) is also an extension of the age-structured model in [26] by introducing sex-structure, and adding classes of vaccinated individuals, vaccinated infectious individuals, and those with persistent infections, in

Variable	Description
$S_m(a,t)$	population of susceptible males
$V_m(a,t)$	population of vaccinated males
$I_m(a,t)$	population of infected (unvaccinated) males
$P_m(a,t)$	population of males with persistent HPV infection
$I_{mv}(a,t)$	population of vaccinated infected males
$P_{mv}(a,t)$	population of vaccinated males with persistent HPV infection
$R_m(a,t)$	population of recovered individuals males
$N_m(a,t)$	total male population
$\mathcal{N}_m(a)$	total male population at demographic stationary state
$S_f(a,t)$	population of susceptible females
$V_f(a,t)$	population of vaccinated females
$I_f(a,t)$	population of infected (unvaccinated) females
$P_f(a,t)$	population of females with persistent HPV infection
$I_{fv}(a,t)$	population of vaccinated infected females
$P_{fv}(a,t)$	population of vaccinated females with persistent HPV infection
$R_f(a,t)$	population of recovered individuals females
$N_f(a,t)$	total female population
$\mathcal{N}_f(a)$	total female population at demographic stationary state

TABLE 1. Description of state variables of the model (2).

both genders respectively. It is worth mentionaing that the model in [26] also accounts for latently-infected and treated individuals. The ODE model in [15] includes vaccine waning but ignores persistent infection. (It should be mentioned that, in [15], an age-structured PDE model was also constructed to study the dynamics of HPV-related complications. The current study does not include the effect of such complications).

3. **Qualitative analysis of the model.** Since the variables R_j $(j = m, f)$ in (2) do not feature in any of the other equations, the equations for R_j can be removed from (2) (these populations can be recovered using the relation $R_j = N_j - S_j - V_j - I_j - P_j - I_{jv} - P_{jv};\ j = m, f$). The model (2) can then be re-written as:

$$\begin{aligned}
\left(\frac{\partial}{\partial a} + \frac{\partial}{\partial t}\right) S_m(a,t) &= -\lambda_m(a,t)S_m(a,t) + \omega_m V_m(a,t) - \psi_m(a)S_m(a,t) \\
&\quad - \mu(a)S_m(a,t), \\
\left(\frac{\partial}{\partial a} + \frac{\partial}{\partial t}\right) V_m(a,t) &= \psi_m(a)S_m(a,t) - \omega_m V_m(a,t) - \theta_{mv}\lambda_m(a,t)V_m(a,t) \\
&\quad - \mu(a)V_m(a,t), \\
\left(\frac{\partial}{\partial a} + \frac{\partial}{\partial t}\right) I_m(a,t) &= \lambda_m(a,t)S_m(a,t) - \rho_m I_m(a,t) - \mu(a)I_m(a,t), \\
\left(\frac{\partial}{\partial a} + \frac{\partial}{\partial t}\right) P_m(a,t) &= q_1\rho_m I_m(a,t) - \kappa_m P_m(a,t) - \mu(a)P_m(a,t), \\
\left(\frac{\partial}{\partial a} + \frac{\partial}{\partial t}\right) I_{mv}(a,t) &= \theta_{mv}\lambda_m(a,t)V_m(a,t) - \rho_{mv} I_{mv}(a,t) - \mu(a)I_{mv}(a,t),
\end{aligned}$$

Parameters	Description
μ^*	*per* capita birth rate
σ	maximum attainable age in the population
$\mu(a)$	age-dependent death rate
N_{m0}	initial size of the total male population
$\psi_m(a)$	age-dependent vaccination rate for males
ω_m	vaccine waning rate for males
ρ_m	rate of development of persistent HPV infection in males
ρ_{mv}	rate of development of persistent HPV infection in vaccinated males
κ_m	recovery rate of males with persistent HPV infection
κ_{mv}	recovery rate of vaccinated males with persistent HPV infection
η_{1m}	infectiousness of unvaccinated males with persistent HPV infection relative to the unvaccinated infectious males
η_{2m}	infectiousness of vaccinated infectious males, relative to the unvaccinated infectious males
η_{3m}	infectiousness of vaccinated males with persistent HPV infection relative to the unvaccinated infectious males
$c_m(a,b)$	average number of female sexual partners of age b for a male of age a
$\beta_m(a,b)$	probability of HPV transmission from an infected female of age b to a susceptible male of age a, *per* contact
q_1	fraction of unvaccinated infected males who develop persistent HPV infection
q_2	fraction of vaccinated infected males who develop persistent HPV infection
N_{f0}	initial size of the total female population
$\psi_f(a)$	age-dependent vaccination rate for females
ω_f	vaccine waning rate for females
ρ_f	rate of development of persistent HPV infection in unvaccinated females
ρ_{fv}	rate of development of persistent HPV infection in vaccinated females
κ_f	recovery rate of females with persistent HPV infection
κ_{fv}	recovery rate of vaccinated females with persistent HPV infection
η_{1f}	infectiousness of unvaccinated females with persistent HPV infection relative to the unvaccinated infectious females
η_{2f}	infectiousness of vaccinated infectious females, relative to the unvaccinated infectious females
η_{3f}	infectiousness of vaccinated females with persistent HPV infection relative to the unvaccinated infectious females
$c_f(a,b)$	average number of male partners of age b for a female of age a
$\beta_f(a,b)$	probability of HPV transmission from an infected male of age b to a susceptible female of age a, *per* contact
p_1	fraction of unvaccinated infected females who develop persistent HPV infection
p_2	fraction of vaccinated infected females who develop persistent HPV infection

TABLE 2. Description of parameters of the model (2)

$$\begin{aligned}
&\left(\frac{\partial}{\partial a}+\frac{\partial}{\partial t}\right)P_{mv}(a,t)=q_2\rho_{mv}I_{mv}(a,t)-\kappa_{mv}P_{mv}(a,t)-\mu(a)P_{mv}(a,t),\\
&\left(\frac{\partial}{\partial a}+\frac{\partial}{\partial t}\right)S_f(a,t)=-\lambda_f(a,t)S_f(a,t)+\omega_f V_f(a,t)-\psi_f(a)S_f(a,t)\\
&\qquad\qquad\qquad\qquad -\mu(a)S_f(a,t),\\
&\left(\frac{\partial}{\partial a}+\frac{\partial}{\partial t}\right)V_f(a,t)=\psi_f(a)S_f(a,t)-\omega_f V_f(a,t)-\theta_{fv}\lambda_f(a,t)V_f(a,t)\\
&\qquad\qquad\qquad\qquad -\mu(a)V_f(a,t),\\
&\left(\frac{\partial}{\partial a}+\frac{\partial}{\partial t}\right)I_f(a,t)=\lambda_f(a,t)S_f(a,t)-\rho_f I_f(a,t)-\mu(a)I_f(a,t),\\
&\left(\frac{\partial}{\partial a}+\frac{\partial}{\partial t}\right)P_f(a,t)=p_1\rho_f I_f(a,t)-\kappa_f P_f(a,t)-\mu(a)P_f(a,t),\\
&\left(\frac{\partial}{\partial a}+\frac{\partial}{\partial t}\right)I_{fv}(a,t)=\theta_{fv}\lambda_f(a,t)V_f(a,t)-\rho_{fv}I_{fv}(a,t)-\mu(a)I_{fv}(a,t),\\
&\left(\frac{\partial}{\partial a}+\frac{\partial}{\partial t}\right)P_{fv}(a,t)=p_2\rho_{fv}I_{fv}(a,t)-\kappa_{fv}P_{fv}(a,t)-\mu(a)P_{fv}(a,t),\\
&S_j(0,t)=\mu^* N_{j0},\ V_j(0,t)=I_j(0,t)=P_j(0,t)=I_{jv}(0,t)\\
&=P_{jv}(0,t)=0;\ j=m,f,
\end{aligned}\tag{8}$$

where,

$$\begin{aligned}
&\lambda_m(a,t)=\\
&C\int_0^\sigma \beta_m(a,b)[I_f(b,t)+\eta_{1f}P_f(b,t)+\eta_{2f}I_{fv}(b,t)+\eta_{3f}P_{fv}(b,t)]db,\\
&\lambda_f(a,t)\\
&=C\int_0^\sigma \beta_f(a,b)[I_m(b,t)+\eta_{1m}P_m(b,t)+\eta_{2m}I_{mv}(b,t)+\eta_{3m}P_{mv}(b,t)]db.
\end{aligned}\tag{9}$$

It can be shown that the PDE system (8) has a unique solution through each given initial data (7) (see, for example, [16, 20, 29]).

3.1. **Existence and stability of equilibria.** The model (8) will be analysed subject to the separable mixing [7, 14] given by

$$\beta_j(a,b)=\beta_j(a)\gamma_j(b),\ \text{ for } j\in\{m,f\}.\tag{10}$$

Using the definition (10) in (9) gives

$$\lambda_m(a,t)=C\beta_m(a)U_m(t),\tag{11}$$

where,

$$U_m(t)=\int_0^\sigma \gamma_m(b)\left[I_f(b,t)+\eta_{1f}P_f(b,t)+\eta_{2f}I_{fv}(b,t)+\eta_{3f}P_{fv}(b,t)\right]db.\tag{12}$$

Similarly,

$$\lambda_f(a,t)=C\beta_f(a)U_f(t),\tag{13}$$

with,

$$U_f(t)=\int_0^\sigma \gamma_f(b)[I_m(b,t)+\eta_{1m}P_m(b,t)+\eta_{2m}I_{mv}(b,t)+\eta_{3m}P_{mv}(b,t)]db.\tag{14}$$

Let,

$$\begin{aligned}\hat{\mathcal{E}} = (&\hat{S}_m(a), \hat{V}_m(a), \hat{I}_m(a), \hat{P}_m(a), \hat{I}_{mv}(a), \hat{P}_{mv}(a),\\ &\hat{S}_f(a), \hat{V}_f(a), \hat{I}_f(a), \hat{P}_f(a), \hat{I}_{fv}(a), \hat{P}_{fv}(a))\end{aligned}$$

be an arbitrary equilibrium solution of the model (8). Then, $\hat{\mathcal{E}}$ satisfies

$$\begin{aligned}
&\frac{d}{da}\hat{S}_m(a) = -\hat{\lambda}_m(a)\hat{S}_m(a) + \omega_m\hat{V}_m(a) - \psi_m(a)\hat{S}_m(a) - \mu(a)\hat{S}_m(a),\\
&\frac{d}{da}\hat{V}_m(a) = \psi_m(a)\hat{S}_m(a) - \omega_m\hat{V}_m(a) - \theta_{mv}\hat{\lambda}_m(a)\hat{V}_m(a) - \mu(a)\hat{V}_m(a),\\
&\frac{d}{da}\hat{I}_m(a) = \hat{\lambda}_m(a)\hat{S}_m(a) - \rho_m\hat{I}_m(a) - \mu(a)\hat{I}_m(a),\\
&\frac{d}{da}\hat{P}_m(a) = q_1\rho_m\hat{I}_m(a) - \kappa_m\hat{P}_m(a) - \mu(a)\hat{P}_m(a),\\
&\frac{d}{da}\hat{I}_{mv}(a) = \theta_{mv}\hat{\lambda}_m(a)\hat{V}_m(a) - \rho_{mv}\hat{I}_{mv}(a) - \mu(a)\hat{I}_{mv}(a),\\
&\frac{d}{da}\hat{P}_{mv}(a) = q_2\rho_{mv}\hat{I}_{mv}(a) - \kappa_{mv}\hat{P}_{mv}(a) - \mu(a)\hat{P}_{mv}(a),\\
&\frac{d}{da}\hat{S}_f(a) = -\hat{\lambda}_f(a)\hat{S}_f(a) + \omega_f\hat{V}_f(a) - \psi_f(a)\hat{S}_f(a) - \mu(a)\hat{S}_f(a),\\
&\frac{d}{da}\hat{V}_f(a) = \psi_f(a)\hat{S}_f(a) - \omega_f\hat{V}_f(a) - \theta_{fv}\hat{\lambda}_f(a)\hat{V}_f(a) - \mu(a)\hat{V}_f(a),\\
&\frac{d}{da}\hat{I}_f(a) = \hat{\lambda}_f(a)\hat{S}_f(a) - \rho_f\hat{I}_f(a) - \mu(a)\hat{I}_f(a),\\
&\frac{d}{da}\hat{P}_f(a) = p_1\rho_f\hat{I}_f(a) - \kappa_f\hat{P}_f(a) - \mu(a)\hat{P}_f(a),\\
&\frac{d}{da}\hat{I}_{fv}(a) = \theta_{fv}\hat{\lambda}_f(a)\hat{V}_f(a) - \rho_{fv}\hat{I}_{fv}(a) - \mu(a)\hat{I}_{fv}(a),\\
&\frac{d}{da}\hat{P}_{fv}(a) = p_2\rho_{fv}\hat{I}_{fv}(a) - \kappa_{fv}\hat{P}_{fv}(a) - \mu(a)\hat{P}_{fv}(a),
\end{aligned} \tag{15}$$

with,

$$\begin{aligned}
&\hat{\lambda}_m(a) = C\beta_m(a)\hat{U}_m,\\
&\qquad \hat{U}_m = \int_0^\sigma \gamma_m(b)[\hat{I}_f(b) + \eta_{1f}\hat{P}_f(b) + \eta_{2f}\hat{I}_{fv} + \eta_{3f}\hat{P}_{fv}(b)]db,\\
&\hat{\lambda}_f(a) = C\beta_f(a)\hat{U}_f,\\
&\qquad \hat{U}_f = \int_0^\sigma \gamma_f(b)[\hat{I}_m(b) + \eta_{1m}\hat{P}_m(b) + \eta_{2m}\hat{I}_{mv} + \eta_{3m}\hat{P}_{mv}(b)]db,
\end{aligned} \tag{16}$$

and, from (6),

$$\begin{aligned}
&\hat{S}_m(0) = \mu^* N_{m0},\ \hat{V}_m(0) = \hat{I}_m(0) = \hat{P}_m(0) = \hat{I}_{mv}(0) = \hat{P}_{mv}(0) = 0,\\
&\hat{S}_f(0) = \mu^* N_{f0},\ \hat{V}_f(0) = \hat{I}_f(0) = \hat{P}_f(0) = \hat{I}_{fv}(0) = \hat{P}_{fv}(0) = 0.
\end{aligned}$$

Solving each equation in (15) gives

$$\begin{aligned}
\hat{S}_m(a) = \omega_m \int_0^a &\hat{V}_m(\xi) e^{-\int_\xi^a [C\beta_m(\tau)\hat{U}_m + \psi_m(\tau) + \mu(\tau)]d\tau} d\xi\\
&+ \mu^* N_{m0}\ e^{-\int_0^a [C\beta_m(\tau)\hat{U}_m + \psi_m(\tau) + \mu(\tau)]d\tau},
\end{aligned} \tag{17}$$

$$\hat{V}_m(a) = \int_0^a \psi_m(\xi)\hat{S}_m(\xi)e^{-\int_\xi^a [\omega_m+\theta_{mv}C\beta_m(\tau)\hat{U}_m+\mu(\tau)]d\tau}d\xi,$$

$$\hat{I}_m(a) = C\hat{U}_m \int_0^a \beta_m(\xi)\hat{S}_m(\xi)e^{\rho_m(\xi-a)-\int_\xi^a \mu(\tau)d\tau}d\xi,$$

$$\hat{P}_m(a) = q_1\rho_m C\hat{U}_m \int_0^a \int_0^\xi \beta_m(\eta)\hat{S}_m(\eta)e^{\rho_m(\eta-\xi)+\kappa_m(\xi-a)-\int_\eta^a \mu(\tau)d\tau}d\eta d\xi,$$

$$\hat{I}_{mv}(a) = \theta_{mv}C\hat{U}_m \int_0^a \beta_m(\xi)\hat{V}_m(\xi)e^{\rho_{mv}(\xi-a)-\int_\xi^a \mu(\tau)d\tau}d\xi,$$

$$\hat{P}_{mv}(a) = q_2\rho_{mv}\theta_{mv}C\hat{U}_m \int_0^a \int_0^\xi \beta_f(\eta)\hat{V}_m(\eta)e^{\rho_{mv}(\eta-\xi)+\kappa_{mv}(\xi-a)-\int_\eta^a \mu(\tau)d\tau}d\eta d\xi,$$

$$\hat{S}_f(a) = \omega_f \int_0^a \hat{V}_f(\xi)e^{-\int_\xi^a [C\beta_f(\tau)\hat{U}_f+\psi_f(\tau)+\mu(\tau)]d\tau}d\xi$$
$$+ \mu^* N_{f0}\ e^{-\int_0^a [C\beta_f(\tau)\hat{U}_f+\psi_f(\tau)+\mu(\tau)]d\tau},$$

$$\hat{V}_f(a) = \int_0^a \psi_f(\xi)\hat{S}_f(\xi)e^{-\int_\xi^a [\omega_f+\theta_{fv}C\beta_f(\tau)\hat{U}_f+\mu(\tau)]d\tau}d\xi,$$

$$\hat{I}_f(a) = C\hat{U}_f \int_0^a \beta_f(\xi)\hat{S}_f(\xi)e^{\rho_f(\xi-a)-\int_\xi^a \mu(\tau)d\tau}d\xi,$$

$$\hat{P}_f(a) = p_1\rho_f C\hat{U}_f \int_0^a \int_0^\xi \beta_f(\eta)\hat{S}_f(\eta)e^{\rho_f(\eta-\xi)+\kappa_f(\xi-a)-\int_\eta^a \mu(\tau)d\tau}d\eta d\xi,$$

$$\hat{I}_{fv}(a) = \theta_{fv}C\hat{U}_f \int_0^a \beta_f(\xi)\hat{V}_f(\xi)e^{\rho_{fv}(\xi-a)-\int_\xi^a \mu(\tau)d\tau}d\xi,$$

$$\hat{P}_{fv}(a) = p_2\rho_{fv}\theta_{fv}C\hat{U}_f \int_0^a \int_0^\xi \beta_f(\eta)\hat{V}_f(\eta)e^{\rho_{fv}(\eta-\xi)+\kappa_{fv}(\xi-a)-\int_\eta^a \mu(\tau)d\tau}d\eta d\xi.$$

3.1.1. *Disease-free equilibrium (DFE).* The system (8) has a DFE, denoted by

$$\mathcal{E}_0 := (S_m^*(a), V_m^*(a), 0, 0, 0, 0, S_f^*(a), V_f^*(a), 0, 0, 0, 0),$$

which corresponds to the solution (17), with $\hat{U}_m = \hat{U}_f = 0$. Setting $\hat{U}_m = \hat{U}_f = 0$ in (17) shows that the steady-state components of the DFE, $S_m^*(a)$, $V_m^*(a)$, $S_f^*(a)$ and $V_f^*(a)$, satisfy

$$S_j^*(a) = \omega_j \int_0^a V_j^*(\xi)e^{-\int_\xi^a [\psi_j(\tau)+\mu(\tau)]d\tau}d\xi + \mu^* N_{j0}\ e^{-\int_0^a [\psi_j(\tau)+\mu(\tau)]d\tau},$$

and,

$$V_j^*(a) = \int_0^a \psi_j(\xi)S_j^*(\xi)e^{-\int_\xi^a [\omega_j+\mu(\tau)]d\tau}d\xi,\ j \in \{m, f\}.$$

The local stability of the DFE ($\mathcal{E}_0$) is investigated by linearizing the system (8) around $\mathcal{E}_0$. Following [13, 21, 22], consider the exponential solutions (perturbations) of the form

$$\begin{aligned}
S_m(a,t) &= S_m^*(a) + \bar{S}_m(a)e^{\lambda t}, & S_f(a,t) &= S_f^*(a) + \bar{S}_f(a)e^{\lambda t},\\
V_m(a,t) &= V_m^*(a) + \bar{V}_m(a)e^{\lambda t}, & V_f(a,t) &= V_f^*(a) + \bar{V}_f(a)e^{\lambda t},\\
I_m(a,t) &= \bar{I}_m(a)e^{\lambda t}, & I_f(a,t) &= \bar{I}_f(a)e^{\lambda t},\\
P_m(a,t) &= \bar{P}_m(a)e^{\lambda t}, & P_f(a,t) &= \bar{P}_f(a)e^{\lambda t},\\
I_{mv}(a,t) &= \bar{I}_{mv}(a)e^{\lambda t}, & I_{fv}(a,t) &= \bar{I}_{fv}(a)e^{\lambda t},\\
P_{mv}(a,t) &= \bar{P}_{mv}(a)e^{\lambda t}, & P_{fv}(a,t) &= \bar{P}_{fv}(a)e^{\lambda t},
\end{aligned} \quad (18)$$

where λ is a real or complex number. Using (18) in (11) and (13) gives

$$\lambda_m(a,t) = C\beta_m(a)U_m^0 e^{\lambda t},\ \ \lambda_f(a,t) = C\beta_f(a)U_f^0 e^{\lambda t}$$

where the constants U_m^0 and U_f^0 are given by

$$U_m^0 = \int_0^\sigma \gamma_m(b)[\bar{I}_f(b) + \eta_{1f}\bar{P}_f(b) + \eta_{2f}\bar{I}_{fv}(b) + \eta_{3f}\bar{P}_{fv}(b)]db, \tag{19}$$

and,

$$U_f^0 = \int_0^\sigma \gamma_f(b)[\bar{I}_m(b) + \eta_{1m}\bar{P}_m(b) + \eta_{2m}\bar{I}_{mv}(b) + \eta_{3m}\bar{P}_{mv}(b)]db. \tag{20}$$

Using (18) in (2), it can be shown that the linear part of (8) is of the form:

$$\begin{aligned}
\frac{d}{da}\bar{S}_m(a) &= -[\lambda + \psi_m(a) + \mu(a)]\bar{S}_m(a) + \omega_m\bar{V}_m(a) - C\beta_m(a)U_m^0 S_m^*(a),\\
\frac{d}{da}\bar{V}_m(a) &= \psi_m(a)\bar{S}_m(a) - [\lambda + \omega_m + \mu(a)]\bar{V}_m(a) - \theta_{mv}C\beta_m(a)U_m^0 V_m^*(a),\\
\frac{d}{da}\bar{I}_m(a) &= -[\lambda + \rho_m + \mu(a)]\bar{I}_m(a) + C\beta_m(a)U_m^0 S_m^*(a),\\
\frac{d}{da}\bar{P}_m(a) &= q_1\rho_m\bar{I}_m(a) - [\lambda + \kappa_m + \mu(a)]\bar{P}_m(a),\\
\frac{d}{da}\bar{I}_{mv}(a) &= -[\lambda + \rho_{mv} + \mu(a)]\bar{I}_m(a) + \theta_{mv}C\beta_m(a)U_m^0 V_m^*(a),\\
\frac{d}{da}\bar{P}_{mv}(a) &= q_2\rho_{mv}\bar{I}_{mv}(a) - [\lambda + \kappa_{mv} + \mu(a)]\bar{P}_{mv}(a),\\
\frac{d}{da}\bar{S}_f(a) &= -[\lambda + \psi_f(a) + \mu(a)]\bar{S}_f(a) + \omega_f\bar{V}_f(a) - C\beta_f(a)U_f^0 S_f^*(a),\\
\frac{d}{da}\bar{V}_f(a) &= \psi_f(a)\bar{S}_f(a) - [\lambda + \omega_f + \mu(a)]\bar{V}_f(a) - \theta_{fv}C\beta_f(a)U_f^0 V_f^*(a),\\
\frac{d}{da}\bar{I}_f(a) &= -[\lambda + \rho_f + \mu(a)]\bar{I}_f(a) + C\beta_f(a)U_f^0 S_f^*(a),\\
\frac{d}{da}\bar{P}_f(a) &= p_1\rho_f\bar{I}_f(a) - [\lambda + \kappa_f + \mu(a)]\bar{P}_f(a),\\
\frac{d}{da}\bar{I}_{fv}(a) &= -[\lambda + \rho_{fv} + \mu(a)]\bar{I}_f(a) + \theta_{fv}C\beta_f(a)U_f^0 V_f^*(a),\\
\frac{d}{da}\bar{P}_{fv}(a) &= p_2\rho_{fv}\bar{I}_{fv}(a) - [\lambda + \kappa_{fv} + \mu(a)]\bar{P}_{fv}(a).
\end{aligned} \tag{21}$$

Solving the equations for the infected classes in (21) gives

$$\begin{aligned}
&\bar{I}_m(a) = CU_m^0\int_0^a \beta_m(\xi)S_m^*(\xi)e^{(\lambda+\rho_m)(\xi-a)-\int_\xi^a \mu(\tau)d\tau}d\xi,\\
&\bar{P}_m(a) =\\
&q_1\rho_m CU_m^0\int_0^a\int_0^\xi \beta_m(\eta)S_m^*(\eta)e^{\lambda(\eta-a)+\rho_m(\eta-\xi)+\kappa_m(\xi-a)-\int_\eta^a \mu(\tau)d\tau}d\eta d\xi,\\
&\bar{I}_{mv}(a) = CU_m^0\theta_{mv}\int_0^a \beta_m(\xi)V_m^*(\xi)e^{(\lambda+\rho_{mv})(\xi-a)-\int_\xi^a \mu(\tau)d\tau}d\xi,\\
&\bar{P}_{mv}(a) =\\
&q_2\rho_{mv}CU_m^0\theta_{mv}\int_0^a\int_0^\xi \beta_m(\eta)V_m^*(\eta)e^{\lambda(\eta-a)+\rho_{mv}(\eta-\xi)+\kappa_{mv}(\xi-a)-\int_\eta^a \mu(\tau)d\tau}d\eta d\xi,
\end{aligned} \tag{22}$$

$$\bar{I}_f(a) = CU_f^0 \int_0^a \beta_f(\xi) S_f^*(\xi) e^{(\lambda+\rho_f)(\xi-a) - \int_\xi^a \mu(\tau)d\tau} d\xi,$$
$$\bar{P}_f(a) = p_1\rho_f CU_f^0 \int_0^a \int_0^\xi \beta_f(\eta) S_f^*(\eta) e^{\lambda(\eta-a)+\rho_f(\eta-\xi)+\kappa_f(\xi-a) - \int_\eta^a \mu(\tau)d\tau} d\eta d\xi,$$
$$\bar{I}_{fv}(a) = CU_f^0\theta_{fv} \int_0^a \beta_f(\xi) V_f^*(\xi) e^{(\lambda+\rho_{fv})(\xi-a) - \int_\xi^a \mu(\tau)d\tau} d\xi,$$
$$\bar{P}_{fv}(a) =$$
$$p_2\rho_{fv} CU_f^0\theta_{fv} \int_0^a \int_0^\xi \beta_f(\eta) V_f^*(\eta) e^{\lambda(\eta-a)+\rho_{fv}(\eta-\xi)+\kappa_{fv}(\xi-a) - \int_\eta^a \mu(\tau)d\tau} d\eta d\xi.$$

Substituting the equations for $\bar{I}_f, \bar{P}_f, \bar{I}_{fv}$ and $\bar{P}_{fv}$ in (22) into the expression for U_m^0 in (19) gives

$$U_m^0 = \tag{23}$$
$$CU_f^0 \left\{ \int_0^\sigma \gamma_m(b) \left[\int_0^b \beta_f(\xi) S_f^*(\xi) e^{(\lambda+\rho_f)(\xi-b) - \int_\xi^b \mu(\tau)d\tau} d\xi \right.\right.$$
$$+ \eta_{1f} p_1 \rho_f \int_0^b \int_0^\xi \beta_f(\eta) S_f^*(\eta) e^{\lambda(\eta-b)+\rho_f(\eta-\xi)+\kappa_f(\xi-b) - \int_\eta^b \mu(\tau)d\tau} d\eta d\xi$$
$$+ \eta_{2f}\theta_{fv} \int_0^b \beta_f(\xi) V_f^*(\xi) e^{(\lambda+\rho_{fv})(\xi-b) - \int_\xi^b \mu(\tau)d\tau} d\xi$$
$$\left.\left. + \eta_{3f} p_2 \rho_{fv}\theta_{fv} \int_0^b \int_0^\xi \beta_f(\eta) V_f^*(\eta) e^{\lambda(\eta-b)+\rho_{fv}(\eta-\xi)+\kappa_{fv}(\xi-b) - \int_\eta^b \mu(\tau)d\tau} d\eta d\xi \right] db \right\}.$$

Similarly, substituting the equations for $\bar{I}_m, \bar{P}_m, \bar{I}_{mv}$ and $\bar{P}_{mv}$ in (22) into the expression for U_f^0 in (20) gives

$$\begin{aligned} U_f^0 = CU_m^0 &\left\{ \int_0^\sigma \gamma_f(b) \left[\int_0^b \beta_m(\xi) S_m^*(\xi) e^{(\lambda+\rho_m)(\xi-b) - \int_\xi^b \mu(\tau)d\tau} d\xi \right.\right. \\ &+ \eta_{1m} q_1 \rho_m \int_0^b \int_0^\xi \beta_m(\eta) S_m^*(\eta) e^{\lambda(\eta-b)+\rho_m(\eta-\xi)+\kappa_m(\xi-b) - \int_\eta^b \mu(\tau)d\tau} d\eta d\xi \\ &+ \eta_{2m}\theta_{mv} \int_0^b \beta_m(\xi) V_m^*(\xi) e^{(\lambda+\rho_{mv})(\xi-b) - \int_\xi^b \mu(\tau)d\tau} d\xi \\ &+ \eta_{3m} q_2 \rho_{mv}\theta_{mv} \\ &\left.\left. \int_0^b \int_0^\xi \beta_m(\eta) V_m^*(\eta) e^{\lambda(\eta-b)+\rho_{mv}(\eta-\xi)+\kappa_{mv}(\xi-b) - \int_\eta^b \mu(\tau)d\tau} d\eta d\xi \right] db \right\}. \end{aligned} \tag{24}$$

Using the expression for U_f^0 in (25) into (23) gives

$$U_m^0 =$$
$$CU_m^0 \left\{ \int_0^\sigma \gamma_f(b) \left[\int_0^b \beta_m(\xi) S_m^*(\xi) e^{(\lambda+\rho_m)(\xi-b) - \int_\xi^b \mu(\tau)d\tau} d\xi \right.\right.$$
$$+ \eta_{1m} q_1 \rho_m \int_0^b \int_0^\xi \beta_m(\eta) S_m^*(\eta) e^{\lambda(\eta-b)+\rho_m(\eta-\xi)+\kappa_m(\xi-b) - \int_\eta^b \mu(\tau)d\tau} d\eta d\xi$$

$$
\begin{aligned}
&+ \eta_{2m}\theta_{mv}\int_0^b \beta_m(\xi)V_m^*(\xi)e^{(\lambda+\rho_{mv})(\xi-b)-\int_\xi^b \mu(\tau)d\tau}d\xi\\
&+ \eta_{3m}q_2\rho_{mv}\theta_{mv}\\
&\int_0^b\int_0^\xi \beta_m(\eta)V_m^*(\eta)e^{\lambda(\eta-b)+\rho_{mv}(\eta-\xi)+\kappa_{mv}(\xi-b)-\int_\eta^b \mu(\tau)d\tau}d\eta d\xi\Bigg] db\Bigg\}\\
&\times C\left\{\int_0^\sigma \gamma_m(b)\left[\int_0^b \beta_f(\xi)S_f^*(\xi)e^{(\lambda+\rho_f)(\xi-b)-\int_\xi^b \mu(\tau)d\tau}d\xi\right.\right.\\
&+ \eta_{1f}p_1\rho_f\int_0^b\int_0^\xi \beta_f(\eta)S_f^*(\eta)e^{\lambda(\eta-b)+\rho_f(\eta-\xi)+\kappa_f(\xi-b)-\int_\eta^b \mu(\tau)d\tau}d\eta d\xi\\
&+ \eta_{2f}\theta_{fv}\int_0^b \beta_f(\xi)V_f^*(\xi)e^{(\lambda+\rho_{fv})(\xi-b)-\int_\xi^b \mu(\tau)d\tau}d\xi\\
&+ \eta_{3f}p_2\rho_{fv}\theta_{fv}\\
&\left.\left.\int_0^b\int_0^\xi \beta_f(\eta)V_f^*(\eta)e^{\lambda(\eta-b)+\rho_{fv}(\eta-\xi)+\kappa_{fv}(\xi-b)-\int_\eta^b \mu(\tau)d\tau}d\eta d\xi\right] db\right\}.
\end{aligned}
\tag{25}
$$

It follows from (**??**) (by dividing both sides by $U_m^0 \neq 0$) that the associated characteristic equation is given by:

$$
G(\lambda) := G_1(\lambda)G_2(\lambda) = 1, \tag{26}
$$

where,

$$
\begin{aligned}
G_1(\lambda) =& C\int_0^\sigma \gamma_f(b)\left[\int_0^b \beta_m(\xi)S_m^*(\xi)e^{(\lambda+\rho_m)(\xi-b)-\int_\xi^b \mu(\tau)d\tau}d\xi\right.\\
&+ \eta_{1m}q_1\rho_m\int_0^b\int_0^\xi \beta_m(\eta)S_m^*(\eta)e^{\lambda(\eta-b)+\rho_m(\eta-\xi)+\kappa_m(\xi-b)-\int_\eta^b \mu(\tau)d\tau}d\eta d\xi\\
&+ \eta_{2m}\theta_{mv}\int_0^b \beta_m(\xi)V_m^*(\xi)e^{(\lambda+\rho_{mv})(\xi-b)-\int_\xi^b \mu(\tau)d\tau}d\xi\\
&+ \eta_{3m}q_2\rho_{mv}\theta_{mv}\\
&\left.\int_0^b\int_0^\xi \beta_m(\eta)V_m^*(\eta)e^{\lambda(\eta-b)+\rho_{mv}(\eta-\xi)+\kappa_{mv}(\xi-b)-\int_\eta^b \mu(\tau)d\tau}d\eta d\xi\right] db,
\end{aligned}
$$

and,

$$
\begin{aligned}
G_2(\lambda) =& C\int_0^\sigma \gamma_m(b)\left[\int_0^b \beta_f(\xi)S_f^*(\xi)e^{(\lambda+\rho_f)(\xi-b)-\int_\xi^b \mu(\tau)d\tau}d\xi\right.\\
&+ \eta_{1f}p_1\rho_f\int_0^b\int_0^\xi \beta_f(\eta)S_f^*(\eta)e^{\lambda(\eta-b)+\rho_f(\eta-\xi)+\kappa_f(\xi-b)-\int_\eta^b \mu(\tau)d\tau}d\eta d\xi\\
&+ \eta_{2f}\theta_{fv}\int_0^b \beta_f(\xi)V_f^*(\xi)e^{(\lambda+\rho_{fv})(\xi-b)-\int_\xi^b \mu(\tau)d\tau}d\xi\\
&+ \eta_{3f}p_2\rho_{fv}\theta_{fv}\\
&\left.\int_0^b\int_0^\xi \beta_f(\eta)V_f^*(\eta)e^{\lambda(\eta-b)+\rho_{fv}(\eta-\xi)+\kappa_{fv}(\xi-b)-\int_\eta^b \mu(\tau)d\tau}d\eta d\xi\right] db.
\end{aligned}
$$

It is convenient to define

$$\mathcal{R}_v = \sqrt{G(0)} = \sqrt{\mathcal{R}_{vm}\mathcal{R}_{vf}},$$

where,

$$\begin{aligned}\mathcal{R}_{vf} = C\Bigg\{\int_0^{\sigma} \gamma_f(b)\Bigg[\int_0^b \beta_m(\xi)S_m^*(\xi)e^{\rho_m(\xi-b)-\int_\xi^b \mu(\tau)d\tau}d\xi \\ + \eta_{1m}q_1\rho_m\int_0^b\int_0^\xi \beta_m(\eta)S_m^*(\eta)e^{\rho_m(\eta-\xi)+\kappa_m(\xi-b)-\int_\eta^b \mu(\tau)d\tau}d\eta d\xi \\ + \eta_{2m}\theta_{mv}\int_0^b \beta_m(\xi)V_m^*(\xi)e^{\rho_{mv}(\xi-b)-\int_\xi^b \mu(\tau)d\tau}d\xi \\ +\eta_{3m}q_2\rho_{mv}\theta_{mv}\int_0^b\int_0^\xi \beta_m(\eta)V_m^*(\eta)e^{\rho_{mv}(\eta-\xi)+\kappa_{mv}(\xi-b)-\int_\eta^b \mu(\tau)d\tau}d\eta d\xi\Bigg]db\Bigg\}\end{aligned}$$

and,

$$\begin{aligned}\mathcal{R}_{vm} = C\Bigg\{\int_0^{\sigma} \gamma_m(b)\Bigg[\int_0^b \beta_f(\xi)S_f^*(\xi)e^{\rho_f(\xi-b)-\int_\xi^b \mu(\tau)d\tau}d\xi \\ + \eta_{1f}p_1\rho_f\int_0^b\int_0^\xi \beta_f(\eta)S_f^*(\eta)e^{\rho_f(\eta-\xi)+\kappa_f(\xi-b)-\int_\eta^b \mu(\tau)d\tau}d\eta d\xi \\ + \eta_{2f}\theta_{fv}\int_0^b \beta_f(\xi)V_f^*(\xi)e^{\rho_{fv}(\xi-b)-\int_\xi^b \mu(\tau)d\tau}d\xi \\ +\eta_{3f}p_2\rho_{fv}\theta_{fv}\int_0^b\int_0^\xi \beta_f(\eta)V_f^*(\eta)e^{\rho_{fv}(\eta-\xi)+\kappa_{fv}(\xi-b)-\int_\eta^b \mu(\tau)d\tau}d\eta d\xi\Bigg]db\Bigg\}.\end{aligned}$$

The quantity $\mathcal{R}_v$ is the *effective reproduction number* (see also [9]) associated with the model (8). It measures the average number of new infections generated by a typical infected individual in a population where some susceptible individuals are vaccinated.

Theorem 3.1. *The DFE ($\mathcal{E}_0$), of the model (8), is locally-asymptotically stable (LAS) if $\mathcal{R}_v < 1$, and unstable if $\mathcal{R}_v > 1$.*

Proof. The proof is based on using the approach in [22]. It can, first of all, be shown (using Leibnitz's differentiation rule [17]) that $G'(\lambda) < 0$ for real λ. Furthermore, $\lim_{\lambda\to\infty} G(\lambda) = 0$ and $\lim_{\lambda\to-\infty} G(\lambda) = \infty$. Thus, the characteristic equation (26) has a unique real solution (denoted by λ^*). If $\mathcal{R}_v = \sqrt{G(0)} > 1$ ($\Leftrightarrow G(0) > 1$), then $\lambda^* > 0$. Hence, the DFE ($\mathcal{E}_0$) is unstable in this case. On the other hand, if $\mathcal{R}_v = \sqrt{G(0)} < 1$ ($\Leftrightarrow G(0) < 1$), then $\lambda^* < 0$. Moreover, by Proposition 1 of the Appendix, λ^* is the dominant root of (26). Thus, in line with [22], the DFE $\mathcal{E}_0$ is LAS if $\mathcal{R}_v < 1$, concluding the proof. □

The effective reproduction number $\mathcal{R}_{vm}(\mathcal{R}_{vf})$ represents the average number of new cases of infection in the male (female) population generated by a primary infectious female (male) in the population. The epidemiological implication of Theorem 3.1 is that the the use of an HPV vaccine can lead to the effective control or elimination of the disease in the population if the use of the vaccine can bring (and maintain) the threshold quantity ($\mathcal{R}_v$) to a value less than unity. Mathematically-speaking, Theorem 3.1 implies that HPV can be eliminated from the population (when $\mathcal{R}_v < 1$) if the initial sizes of the sub-populations of the model are in the basin of attraction of the DFE ($\mathcal{E}_0$) (in line with Al-Arydah and Smith? [1]). To ensure that disease elimination is independent of the initial sizes of the sub-populations of the model, it is necessary to show that the DFE is globally-asymptotically stable (GAS). This is considered below.

Theorem 3.2. *The DFE ($\mathcal{E}_0$), of the model (8), is GAS if $\mathcal{R}_v < 1$ and*

$$\limsup_{t\to\infty} S_m(a,t) \le S_m^*(a), \limsup_{t\to\infty} V_m(a,t) \le V_m^*(a),$$
$$\limsup_{t\to\infty} S_f(a,t) \le S_f^*(a), \limsup_{t\to\infty} V_f(a,t) \le V_f^*(a).$$

Proof. The approach in [22] will be used to establish the global stability of the DFE of the model (8). Integrating each equation for the infected classes in (8), along the characteristic lines, gives (for $t > a$)

$$\begin{aligned}
&I_m(a,t) = C\int_0^a \beta_m(\xi)U_m(t-a+\xi)S_m(\xi,t-a+\xi)e^{\rho_m(\xi-a)-\int_\xi^a \mu(\tau)d\tau}d\xi,\\
&P_m(a,t) = q_1\rho_m C\\
&\int_0^a\int_0^\xi \beta_m(\eta)U_m(t-a+\eta)S_m(\eta,t-a+\eta)e^{\rho_m(\eta-\xi)+\kappa_m(\xi-a)-\int_\eta^a \mu(\tau)d\tau}d\eta d\xi,\\
&I_{mv}(a,t) = \theta_{mv}C\int_0^a \beta_m(\xi)U_m(t-a+\xi)V_m(\xi,t-a+\xi)e^{\rho_{mv}(\xi-a)-\int_\xi^a \mu(\tau)d\tau}d\xi,\\
&P_{mv}(a,t) = q_2\rho_{mv}\theta_{mv}C\\
&\int_0^a\int_0^\xi \beta_m(\eta)U_m(t-a+\eta)V_m(\eta,t-a+\eta)e^{\rho_{mv}(\eta-\xi)+\kappa_{mv}(\xi-a)-\int_\eta^a \mu(\tau)d\tau}d\eta d\xi,\\
&I_f(a,t) = C\int_0^a \beta_f(\xi)U_f(t-a+\xi)S_f(\xi,t-a+\xi)e^{\rho_f(\xi-a)-\int_\xi^a \mu(\tau)d\tau}d\xi,\\
&P_f(a,t) = p_1\rho_f C\\
&\int_0^a\int_0^\xi \beta_f(\eta)U_f(t-a+\eta)S_f(\eta,t-a+\eta)e^{\rho_f(\eta-\xi)+\kappa_f(\xi-a)-\int_\eta^a \mu(\tau)d\tau}d\eta d\xi,\\
&I_{fv}(a,t) = \theta_{fv}C\int_0^a \beta_f(\xi)U_f(t-a+\xi)V_f(\xi,t-a+\xi)e^{\rho_{fv}(\xi-a)-\int_\xi^a \mu(\tau)d\tau}d\xi,\\
&P_{fv}(a,t) = p_2\rho_{fv}\theta_{fv}C\\
&\int_0^a\int_0^\xi \beta_f(\eta)U_f(t-a+\eta)V_f(\eta,t-a+\eta)e^{\rho_{fv}(\eta-\xi)+\kappa_{fv}(\xi-a)-\int_\eta^a \mu(\tau)d\tau}d\eta d\xi.
\end{aligned} \tag{27}$$

Using (27) in (12) and (14) gives (for $t > b$)

$$\begin{aligned}
&U_m(t) =\\
&C\ \Bigg\{\int_0^\sigma \gamma_m(b)\Bigg[\int_0^b \beta_f(\xi)U_f(t-b+\xi)S_f(\xi,t-b+\xi)e^{\rho_f(\xi-b)-\int_\xi^b \mu(\tau)d\tau}d\xi\\
&+\eta_{1f}p_1\rho_f\\
&\int_0^b\int_0^\xi \beta_f(\eta)U_f(t-b+\eta)S_f(\eta,t-b+\eta)e^{\rho_f(\eta-\xi)+\kappa_f(\xi-b)-\int_\eta^b \mu(\tau)d\tau}d\eta d\xi
\end{aligned} \tag{28}$$

$$+ \eta_{2f}\theta_{fv}\int_0^b \beta_f(\xi)U_f(t-b+\xi)V_f(\xi,t-b+\xi)e^{\rho_{fv}(\xi-b)-\int_\xi^b \mu(\tau)d\tau}d\xi$$
$$+ \eta_{3f}p_2\rho_{fv}\theta_{fv}\int_0^b\int_0^\xi$$
$$\left.\left.\beta_f(\eta)U_f(t-b+\eta)V_f(\eta,t-b+\eta)e^{\rho_{fv}(\eta-\xi)+\kappa_{fv}(\xi-b)-\int_\eta^b \mu(\tau)d\tau}d\eta d\xi\right] db\right\},$$

and,

$$\begin{aligned}
&U_f(t) = \\
&C\ \left\{\int_0^\sigma \gamma_f(b)\left[\int_0^b \beta_m(\xi)U_m(t-b+\xi)S_m(\xi,t-b+\xi)e^{\rho_m(\xi-b)-\int_\xi^b \mu(\tau)d\tau}d\xi\right.\right. \\
&+ \eta_{1m}q_1\rho_m \\
&\int_0^b\int_0^\xi \beta_m(\eta)U_m(t-b+\eta)S_m(\eta,t-b+\eta)e^{\rho_m(\eta-\xi)+\kappa_m(\xi-b)-\int_\eta^b \mu(\tau)d\tau}d\eta d\xi \\
&+ \eta_{2m}\theta_{mv}\int_0^b \beta_m(\xi)U_m(t-b+\xi)V_m(\xi,t-b+\xi)e^{\rho_{mv}(\xi-b)-\int_\xi^b \mu(\tau)d\tau}d\xi \\
&+ \eta_{3m}q_2\rho_{mv}\theta_{mv}\int_0^b\int_0^\xi \\
&\quad\left.\left.\beta_m(\eta)U_m(t-b+\eta)V_m(\eta,t-b+\eta)e^{\rho_{mv}(\eta-\xi)+\kappa_{mv}(\xi-b)-\int_\eta^b \mu(\tau)d\tau}d\eta d\xi\right] db\right\}.
\end{aligned} \tag{29}$$

Let,

$$F_m(a) = \beta_m(a)\limsup_{t\to\infty} U_m(t),\ \ F_f(a) = \beta_f(a)\limsup_{t\to\infty} U_f(t).$$

Following [21, 22], taking limsup on the two sides of (28) and (29) as $t\to\infty$, and applying Fatou's Lemma, gives

$$\begin{aligned}
&F_m(a) \le \\
&C\beta_m(a)\left\{\int_0^\sigma \gamma_m(b)\left[\int_0^b F_f(\xi)S_f^*(\xi)e^{\rho_f(\xi-b)-\int_\xi^b \mu(\tau)d\tau}d\xi\right.\right. \\
&+ \eta_{1f}p_1\rho_f\int_0^b\int_0^\xi F_f(\eta)S_f^*(\eta)e^{\rho_f(\eta-\xi)+\kappa_f(\xi-b)-\int_\eta^b \mu(\tau)d\tau}d\eta d\xi \\
&+ \eta_{2f}\theta_{fv}\int_0^b F_f(\xi)V_f^*(\xi)e^{\rho_{fv}(\xi-b)-\int_\xi^b \mu(\tau)d\tau}d\xi \\
&\left.\left.+\eta_{3f}p_2\rho_{fv}\theta_{fv}\int_0^b\int_0^\xi F_f(\eta)V_f^*(\eta)e^{\rho_{fv}(\eta-\xi)+\kappa_{fv}(\xi-b)-\int_\eta^b \mu(\tau)d\tau}d\eta d\xi\right] db\right\},
\end{aligned} \tag{30}$$

and,

$$\begin{aligned}
&F_f(a) \le \\
&C\beta_f(a)\left\{\int_0^\sigma \gamma_f(b)\left[\int_0^b F_m(\xi)S_m^*(\xi)e^{\rho_m(\xi-b)-\int_\xi^b \mu(\tau)d\tau}d\xi\right.\right.
\end{aligned}$$

$$
\begin{aligned}
&+ \eta_{1m} q_1 \rho_m \int_0^b \int_0^\xi F_m(\eta) S_m^*(\eta) e^{\rho_m(\eta-\xi)+\kappa_m(\xi-b)-\int_\eta^b \mu(\tau)d\tau} d\eta d\xi \\
&+ \eta_{2m} \theta_{mv} \int_0^b F_m(\xi) V_m^*(\xi) e^{\rho_{mv}(\xi-b)-\int_\xi^b \mu(\tau)d\tau} d\xi \\
&+\eta_{3m} q_2 \rho_{mv} \theta_{mv} \int_0^b \int_0^\xi F_m(\eta) V_m^*(\eta) e^{\rho_{mv}(\eta-\xi)+\kappa_{mv}(\xi-b)-\int_\eta^b \mu(\tau)d\tau} d\eta d\xi \Bigg] db \Bigg\}.
\end{aligned} \tag{31}
$$

It is convenient to define the non-negative constants C_1 and C_2 by

$$
\begin{aligned}
C_1 =& C \int_0^\sigma \gamma_m(b) \Bigg[\int_0^b F_f(\xi) S_f^*(\xi) e^{\rho_f(\xi-b)-\int_\xi^b \mu(\tau)d\tau} d\xi \\
&+ \eta_{1f} p_1 \rho_f \int_0^b \int_0^\xi F_f(\eta) S_f^*(\eta) e^{\rho_f(\eta-\xi)+\kappa_f(\xi-b)-\int_\eta^b \mu(\tau)d\tau} d\eta d\xi \\
&+ \eta_{2f} \theta_{fv} \int_0^b F_f(\xi) V_f^*(\xi) e^{\rho_{fv}(\xi-b)-\int_\xi^b \mu(\tau)d\tau} d\xi \\
&+\eta_{3f} p_2 \rho_{fv} \theta_{fv} \int_0^b \int_0^\xi F_f(\eta) V_f^*(\eta) e^{\rho_{fv}(\eta-\xi)+\kappa_{fv}(\xi-b)-\int_\eta^b \mu(\tau)d\tau} d\eta d\xi \Bigg] db,
\end{aligned} \tag{32}
$$

and,

$$
\begin{aligned}
C_2 =& C \int_0^\sigma \gamma_f(b) \Bigg[\int_0^b F_m(\xi) S_m^*(\xi) e^{\rho_m(\xi-b)-\int_\xi^b \mu(\tau)d\tau} d\xi \\
&+ \eta_{1m} q_1 \rho_m \int_0^b \int_0^\xi F_m(\eta) S_m^*(\eta) e^{\rho_m(\eta-\xi)+\kappa_m(\xi-b)-\int_\eta^b \mu(\tau)d\tau} d\eta d\xi \\
&+ \eta_{2m} \theta_{mv} \int_0^b F_m(\xi) V_m^*(\xi) e^{\rho_{mv}(\xi-b)-\int_\xi^b \mu(\tau)d\tau} d\xi \\
&+\eta_{3m} q_2 \rho_{mv} \theta_{mv} \int_0^b \int_0^\xi F_m(\eta) V_m^*(\eta) e^{\rho_{mv}(\eta-\xi)+\kappa_{mv}(\xi-b)-\int_\eta^b \mu(\tau)d\tau} d\eta d\xi \Bigg] db.
\end{aligned} \tag{33}
$$

Hence (using (32) and (33)), the inequalities (30) and (31) can, respectively, be written as

$$
F_m(a) \le \beta_m(a) C_1 \text{ and } F_f(a) \le \beta_f(a) C_2. \tag{34}
$$

Thus, using (34) in (32) and (33) gives, respectively,

$$
\begin{aligned}
C_1 \le& C \int_0^\sigma \gamma_m(b) \Bigg[\int_0^b \beta_f(\xi) C_2 S_f^*(\xi) e^{\rho_f(\xi-b)-\int_\xi^b \mu(\tau)d\tau} d\xi \\
&+ \eta_{1f} p_1 \rho_f \int_0^b \int_0^\xi \beta_f(\eta) C_2 S_f^*(\eta) e^{\rho_f(\eta-\xi)+\kappa_f(\xi-b)-\int_\eta^b \mu(\tau)d\tau} d\eta d\xi \\
&+ \eta_{2f} \theta_{fv} \int_0^b \beta_f(\xi) C_2 V_f^*(\xi) e^{\rho_{fv}(\xi-b)-\int_\xi^b \mu(\tau)d\tau} d\xi \\
&+\eta_{3f} p_2 \rho_{fv} \theta_{fv} \int_0^b \int_0^\xi \beta_f(\eta) C_2 V_f^*(\eta) e^{\rho_{fv}(\eta-\xi)+\kappa_{fv}(\xi-b)-\int_\eta^b \mu(\tau)d\tau} d\eta d\xi \Bigg] db,
\end{aligned} \tag{35}
$$

and,

$$
\begin{aligned}
C_2 \le& C \int_0^\sigma \gamma_f(b) \left[\int_0^b \beta_m(\xi) C_1 S_m^*(\xi) e^{\rho_m(\xi-b)-\int_\xi^b \mu(\tau)d\tau} d\xi \right. \\
&+ \eta_{1m} q_1 \rho_m \int_0^b \int_0^\xi \beta_m(\eta) C_1 S_m^*(\eta) e^{\rho_m(\eta-\xi)+\kappa_m(\xi-b)-\int_\eta^b \mu(\tau)d\tau} d\eta d\xi \\
&+ \eta_{2m} \theta_{mv} \int_0^b \beta_m(\xi) C_1 V_m^*(\xi) e^{\rho_{mv}(\xi-b)-\int_\xi^b \mu(\tau)d\tau} d\xi \\
&+ \eta_{3m} q_2 \rho_{mv} \theta_{mv} \\
&\left. \int_0^b \int_0^\xi \beta_m(\eta) C_1 V_m^*(\eta) e^{\rho_{mv}(\eta-\xi)+\kappa_{mv}(\xi-b)-\int_\eta^b \mu(\tau)d\tau} d\eta d\xi \right] db,
\end{aligned}
\tag{36}
$$

so that,

$$
\begin{aligned}
C_1 C_2 \le& C \left\{ \int_0^\sigma \gamma_m(b) \left[\int_0^b \beta_f(\xi) C_2 S_f^*(\xi) e^{\rho_f(\xi-b)-\int_\xi^b \mu(\tau)d\tau} d\xi \right. \right. \\
&+ \eta_{1f} p_1 \rho_f \int_0^b \int_0^\xi \beta_f(\eta) C_2 S_f^*(\eta) e^{\rho_f(\eta-\xi)+\kappa_f(\xi-b)-\int_\eta^b \mu(\tau)d\tau} d\eta d\xi \\
&+ \eta_{2f} \theta_{fv} \int_0^b \beta_f(\xi) C_2 V_f^*(\xi) e^{\rho_{fv}(\xi-b)-\int_\xi^b \mu(\tau)d\tau} d\xi \\
&+ \eta_{3f} p_2 \rho_{fv} \theta_{fv} \\
&\left.\left. \int_0^b \int_0^\xi \beta_f(\eta) C_2 V_f^*(\eta) e^{\rho_{fv}(\eta-\xi)+\kappa_{fv}(\xi-b)-\int_\eta^b \mu(\tau)d\tau} d\eta d\xi \right] db \right\} \\
&\times C \left\{ \int_0^\sigma \gamma_f(b) \left[\int_0^b \beta_m(\xi) C_1 S_m^*(\xi) e^{\rho_m(\xi-b)-\int_\xi^b \mu(\tau)d\tau} d\xi \right. \right. \\
&+ \eta_{1m} q_1 \rho_m \int_0^b \int_0^\xi \beta_m(\eta) C_1 S_m^*(\eta) e^{\rho_m(\eta-\xi)+\kappa_m(\xi-b)-\int_\eta^b \mu(\tau)d\tau} d\eta d\xi \\
&+ \eta_{2m} \theta_{mv} \int_0^b \beta_m(\xi) C_1 V_m^*(\xi) e^{\rho_{mv}(\xi-b)-\int_\xi^b \mu(\tau)d\tau} d\xi \\
&+ \eta_{3m} q_2 \rho_{mv} \theta_{mv} \\
&\left.\left. \int_0^b \int_0^\xi \beta_m(\eta) C_1 V_m^*(\eta) e^{\rho_{mv}(\eta-\xi)+\kappa_{mv}(\xi-b)-\int_\eta^b \mu(\tau)d\tau} d\eta d\xi \right] db \right\}, \\
&= C_1 C_2 \mathcal{R}_v^2.
\end{aligned}
\tag{37}
$$

It follows from the inequality (37) that $C_1 = 0$ or $C_2 = 0$ if $\mathcal{R}_v < 1$. If $C_2 = 0$, then $C_1 = 0$ by (35) (since C_1 is non-negative). Similarly, if $C_1 = 0$ then $C_2 = 0$ by (36). Hence, if $\mathcal{R}_v < 1$, then $C_1 = C_2 = 0$. Therefore, $F_m(a) = F_f(a) = 0$. Thus,

$$
\limsup_{t\to\infty} U_m(t) = \limsup_{t\to\infty} U_f(t) = 0. \tag{38}
$$

Using (38) in (27) shows that

$$
\begin{aligned}
&\lim_{t\to\infty} I_m(a,t) = \lim_{t\to\infty} P_m(a,t) = \lim_{t\to\infty} I_{mv}(a,t) = \lim_{t\to\infty} P_{mv}(a,t) = 0, \\
&\lim_{t\to\infty} I_f(a,t) = \lim_{t\to\infty} P_f(a,t) = \lim_{t\to\infty} I_{fv}(a,t) = \lim_{t\to\infty} P_{fv}(a,t) = 0.
\end{aligned}
\tag{39}
$$

Furthermore, since

$$S_j(a,t)+V_j(a,t)+I_j(a,t)+P_j(a,t)+I_{jv}(a,t)+P_{jv}(a,t)=N_j(a,t),\ j\in\{m,f\},$$

it follows (using (39)) that

$$\lim_{t\to\infty}[S_j(a,t)+V_j(a,t)]=\mathcal{N}_j(a),\ \text{for } j\in\{m,f\}.$$

This concludes the proof. □

The DFE of the model (8) is shown to be GAS if the hypotheses of Theorem hold (global-asymptotic stability of the DFE is not established in [1]).

3.1.2. *Endemic equilibrium point (EEP).* The approach in [21] will be used to find conditions for the existence of endemic equilibria of the model (8) (that is, equilibria where the infected components of the model (8) are non-zero), as follows.

Using (17) in (16) gives

$$\begin{aligned}\hat{U}_m=&\int_0^\sigma \gamma_m(b)\Bigg[\hat{U}_f\int_0^b \beta_f(\xi)\hat{S}_f(\xi)e^{\rho_f(\xi-b)-\int_\xi^b\mu(\tau)d\tau}d\xi\\&+\eta_{1f}p_1\rho_f\hat{U}_f\int_0^b\int_0^\xi \beta_f(\eta)\hat{S}_f(\eta)e^{\rho_f(\eta-\xi)+\kappa_f(\xi-b)-\int_\eta^b\mu(\tau)d\tau}d\eta d\xi\\&+\eta_{2f}\theta_{fv}\hat{U}_f\int_0^b \beta_f(\xi)\hat{V}_f(\xi)e^{\rho_{fv}(\xi-b)-\int_\xi^b\mu(\tau)d\tau}d\xi\\&+\eta_{3f}p_2\rho_{fv}\theta_{fv}\hat{U}_f\int_0^b\int_0^\xi \beta_f(\eta)\hat{V}_f(\eta)e^{\rho_{fv}(\eta-\xi)+\kappa_{fv}(\xi-b)-\int_\eta^b\mu(\tau)d\tau}d\eta d\xi\Bigg]db\\=:&\hat{U}_fH_1(\hat{U}_f),\end{aligned}\tag{40}$$

and,

$$\begin{aligned}\hat{U}_f=&\int_0^\sigma \gamma_f(b)\Bigg[\hat{U}_m\int_0^b \beta_m(\xi)\hat{S}_m(\xi)e^{\rho_m(\xi-b)-\int_\xi^b\mu(\tau)d\tau}d\xi\\&+\eta_{1m}q_1\rho_m\hat{U}_m\int_0^b\int_0^\xi \beta_m(\eta)\hat{S}_m(\eta)e^{\rho_m(\eta-\xi)+\kappa_m(\xi-b)-\int_\eta^b\mu(\tau)d\tau}d\eta d\xi\\&+\eta_{2m}\theta_{mv}\hat{U}_m\int_0^b \beta_m(\xi)\hat{V}_m(\xi)e^{\rho_{mv}(\xi-b)-\int_\xi^b\mu(\tau)d\tau}d\xi\\&+\eta_{3m}q_2\rho_{mv}\theta_{mv}\hat{U}_m\\&\int_0^b\int_0^\xi \beta_m(\eta)\hat{V}_m(\eta)e^{\rho_{mv}(\eta-\xi)+\kappa_{mv}(\xi-b)-\int_\eta^b\mu(\tau)d\tau}d\eta d\xi\Bigg]db\\=:&\hat{U}_mH_2(\hat{U}_m).\end{aligned}\tag{41}$$

The model (8) has an EEP if and only if (40) and (41) have a solution $(\hat{U}_m,\hat{U}_f)\neq(0,0)$.

Using (41) in (40) gives,

$$\hat{U}_m=\hat{U}_mH_2(\hat{U}_m)H_1(\hat{U}_mH_2(\hat{U}_m)).\tag{42}$$

Equation (42) has a solution $\hat{U}_m=0$, or a $\hat{U}_m>0$ that satisfies

$$1=H_2(\hat{U}_m)H_1(\hat{U}_mH_2(\hat{U}_m)).\tag{43}$$

It should be noted from (17) that $\hat{S}_m$ and $\hat{V}_m$ are continuous functions of $\hat{U}_m$. Similarly, $\hat{S}_f$ and $\hat{V}_f$ are continuous functions of $\hat{U}_f$. Thus, H_1 and H_2 are continuous functions of $\hat{U}_f$ and $\hat{U}_m$ respectively.

Since $\mathcal{R}_v > 1$, assume (without loosing generality), that $\mathcal{R}_{vf} > 1$. Therefore,

$$H_2(0) = \mathcal{R}_{vf} > 1. \tag{44}$$

For $\hat{U}_m > 0$, (41) gives,

$$H_2(\hat{U}_m) = \frac{\hat{U}_f}{\hat{U}_m}. \tag{45}$$

Using the definition in (16) into (45) gives

$$H_2(\hat{U}_m) = \frac{1}{\hat{U}_m}\int_0^{\sigma} \gamma_f(b)\left[\hat{I}_m(b) + \eta_{1m}\hat{P}_m(b) + \eta_{2m}\hat{I}_{mv} + \eta_{3m}\hat{P}_{mv}(b)\right] db. \tag{46}$$

Since $0 < \eta_{1m}, \eta_{2m}, \eta_{3m} < 1$, it follows that

$$\hat{I}_m(b) + \eta_{1m}\hat{P}_m(b) + \eta_{2m}\hat{I}_{mv} + \eta_{3m}\hat{P}_{mv}(b) < \hat{I}_m(b) + \hat{P}_m(b) + \hat{I}_{mv} + \hat{P}_{mv}(b) < \mathcal{N}_m(b). \tag{47}$$

Let,

$$\gamma_f^+ = \sup_{[0,\infty)} \gamma_f(b).$$

It follows from (1), (46) and (47), that

$$H_2(\hat{U}_m) < \frac{\gamma_f^+}{\hat{U}_m}\int_0^{\sigma} \mathcal{N}_m(b)db = \frac{\gamma_f^+ N_{m0}}{\hat{U}_m},$$

so that, for the case with $\hat{U}_m = \gamma_f^+ N_{m0}$,

$$H_2(\hat{U}_m) < 1.$$

Hence, it can be concluded from the above analyses that if $\mathcal{R}_{vf} > 1$ (so that $H_2(0) > 1$ by (44)), then there is at least one $\hat{U}_m$ in $(0, \gamma_f^+ N_{m0})$, for which equation (43) holds (i.e., (43) has a positive solution). This solution may not be unique, since the right side of (43) may not be monotone (this is because H_1 depends on $\hat{S}_f$ and $\hat{V}_f$, and H_2 depends on $\hat{S}_m$ and $\hat{V}_m$, where $\hat{S}_f, \hat{V}_f, \hat{S}_m, \hat{V}_m$ are defined implicitly). Define now, $\hat{U}_f^* = \hat{U}_m^* H_2(\hat{U}_m^*)$. It is easy to see that $(\hat{U}_m^*, \hat{U}_f^*)$ satisfies (40) and (41).

Let the corresponding equilibrium of the model (8) be denoted by

$$\begin{aligned}\mathcal{E}_1 = (&\tilde{S}_m(a), \tilde{V}_m(a), \tilde{I}_m(a), \tilde{P}_m(a), \tilde{I}_{mv}(a), \tilde{P}_{mv}(a),\\ &\tilde{S}_f(a), \tilde{V}_f(a), \tilde{I}_f(a), \tilde{P}_f(a), \tilde{I}_{fv}(a), \tilde{P}_{fv}(a)).\end{aligned}$$

Thus, the following result is established.

Theorem 3.3. *The model (8) has at least one endemic equilibrium point, of the form $\mathcal{E}_1$, whenever $\mathcal{R}_v > 1$.*

It should be mentioned that a similar result is established for the models considered in [3, 21]. However, unlike in Elbasha [9] where it was shown that the two-sex ODE model for HPV spread in the presence of an imperfect vaccine has a unique endemic equilibrium when the effective reproduction threshold exceeds unity, the above result (Theorem 3.3) shows that adding age-structure to the two-sex ODE model for HPV with an imperfect vaccine could result in the existence of multiple endemic equilibria when the effective reproduction threshold is greater than unity (since the nonlinear equation (43) may have more than one positive solutions, and, in turn, (40) and (41) may have multiple positive solutions).

Conclusions. A new age-structured two-sex model is designed and used to study the transmission dynamics of human pappilomavirus in the presence of an imperfect anti-HPV vaccine. The main theoretical results shown are summarized below:

(i) The disease-free equilibrium of the model is locally-asymptotically stable whenever the effective reproduction number ($\mathcal{R}_v$) is less than unity. It is globally-asymptotically stable under certain additional conditions;

(ii) The model has at least one endemic equilibrium when the reproduction threshold ($\mathcal{R}_v$) exceeds unity.

Furthermore, the study shows that adding age-structure to the ODE model for HPV spread in the presence of an imperfect vaccine could introduce multiple endemic equilibria (as against the unique endemic equilibrium shown in [9]) when the reproduction threshold exceeds unity.

Appendix.

Proposition 1. *λ^* is the dominant real root of (26).*

Proof. The proof is based on showing that all other roots of the characteristic equation (26) are complex with real part smaller than λ^*. Let (in line with [22]) $\lambda^\dagger = x + iy$ be an arbitrary complex solution of (26). Thus, it follows from (26) that

$$
\begin{aligned}
G(\lambda^*) &= 1 = ReG(\lambda^\dagger) = ReG(x+iy) \\
&= Re\{G_1(x+iy)G_2(x+iy)\} \\
&= Re\ C^2 \Bigg\{ \int_0^\sigma \gamma_f(b) \Bigg[\int_0^b \beta_m(\xi) S_m^*(\xi) e^{(x+iy+\rho_m)(\xi-b) - \int_\xi^b \mu(\tau)d\tau} d\xi \\
&+ \eta_{1m} q_1 \rho_m \int_0^b \int_0^\xi \beta_m(\eta) S_m^*(\eta) e^{(x+iy)(\eta-b)+\rho_m(\eta-\xi)+\kappa_m(\xi-b) - \int_\eta^b \mu(\tau)d\tau} d\eta d\xi \\
&+ \eta_{2m}\theta_{mv} \int_0^b \beta_m(\xi) V_m^*(\xi) e^{(x+iy+\rho_{mv})(\xi-b) - \int_\xi^b \mu(\tau)d\tau} d\xi \\
&+ \eta_{3m} q_2 \rho_{mv} \theta_{mv} \\
&\int_0^b \int_0^\xi \beta_m(\eta) V_m^*(\eta) e^{(x+iy)(\eta-b)+\rho_{mv}(\eta-\xi)+\kappa_{mv}(\xi-b) - \int_\eta^b \mu(\tau)d\tau} d\eta d\xi \Bigg] db \\
&\times \int_0^\sigma \gamma_m(b) \Bigg[\int_0^b \beta_f(\xi) S_f^*(\xi) e^{(x+iy+\rho_f)(\xi-b) - \int_\xi^b \mu(\tau)d\tau} d\xi \\
&+ \eta_{1f} p_1 \rho_f \int_0^b \int_0^\xi \beta_f(\eta) S_f^*(\eta) e^{(x+iy)(\eta-b)+\rho_f(\eta-\xi)+\kappa_f(\xi-b) - \int_\eta^b \mu(\tau)d\tau} d\eta d\xi \\
&+ \eta_{2f}\theta_{fv} \int_0^b \beta_f(\xi) V_f^*(\xi) e^{(x+iy+\rho_{fv})(\xi-b) - \int_\xi^b \mu(\tau)d\tau} d\xi \\
&+ \eta_{3f} p_2 \rho_{fv} \theta_{fv} \\
&\int_0^b \int_0^\xi \beta_f(\eta) V_f^*(\eta) e^{(x+iy)(\eta-b)+\rho_{fv}(\eta-\xi)+\kappa_{fv}(\xi-b) - \int_\eta^b \mu(\tau)d\tau} d\eta d\xi \Bigg] db \Bigg\},
\end{aligned}
$$

$$= C^2 \Bigg\{ \int_0^\sigma \gamma_f(b) \Bigg[\int_0^b \beta_m(\xi) S_m^*(\xi) e^{(x+\rho_m)(\xi-b)-\int_\xi^b \mu(\tau)d\tau} \cos y(\xi-b) d\xi$$

$$+ \eta_{1m} q_1 \rho_m$$

$$\int_0^b \int_0^\xi \beta_m(\eta) S_m^*(\eta) e^{x(\eta-b)+\rho_m(\eta-\xi)+\kappa_m(\xi-b)-\int_\eta^b \mu(\tau)d\tau} \cos y(\eta-b) d\eta d\xi$$

$$+ \eta_{2m} \theta_{mv} \int_0^b \beta_m(\xi) V_m^*(\xi) e^{(x+\rho_{mv})(\xi-b)-\int_\xi^b \mu(\tau)d\tau} \cos y(\xi-b) d\xi$$

$$+ \eta_{3m} q_2 \rho_{mv} \theta_{mv}$$

$$\int_0^b \int_0^\xi \beta_m(\eta) V_m^*(\eta) e^{x(\eta-b)+\rho_{mv}(\eta-\xi)+\kappa_{mv}(\xi-b)-\int_\eta^b \mu(\tau)d\tau} \cos y(\eta-b) d\eta d\xi \Bigg] db$$

$$\times \int_0^\sigma \gamma_m(b) \Bigg[\int_0^b \beta_f(\xi) S_f^*(\xi) e^{(x+\rho_f)(\xi-b)-\int_\xi^b \mu(\tau)d\tau} \cos y(\xi-b) d\xi$$

$$+ \eta_{1f} p_1 \rho_f$$

$$\int_0^b \int_0^\xi \beta_f(\eta) S_f^*(\eta) e^{x(\eta-b)+\rho_f(\eta-\xi)+\kappa_f(\xi-b)-\int_\eta^b \mu(\tau)d\tau} \cos y(\eta-b) d\eta d\xi$$

$$+ \eta_{2f} \theta_{fv} \int_0^b \beta_f(\xi) V_f^*(\xi) e^{(x+\rho_{fv})(\xi-b)-\int_\xi^b \mu(\tau)d\tau} \cos y(\xi-b) d\xi$$

$$+ \eta_{3f} p_2 \rho_{fv} \theta_{fv}$$

$$\int_0^b \int_0^\xi \beta_f(\eta) V_f^*(\eta) e^{x(\eta-b)+\rho_{fv}(\eta-\xi)+\kappa_{fv}(\xi-b)-\int_\eta^b \mu(\tau)d\tau} \cos y(\eta-b) d\eta d\xi \Bigg] db \Bigg\},$$

$$\le C^2 \Bigg\{ \int_0^\sigma \gamma_f(b) \Bigg[\int_0^b \beta_m(\xi) S_m^*(\xi) e^{(x+\rho_m)(\xi-b)-\int_\xi^b \mu(\tau)d\tau} d\xi$$

$$+ \eta_{1m} q_1 \rho_m \int_0^b \int_0^\xi \beta_m(\eta) S_m^*(\eta) e^{x(\eta-b)+\rho_m(\eta-\xi)+\kappa_m(\xi-b)-\int_\eta^b \mu(\tau)d\tau} d\eta d\xi$$

$$+ \eta_{2m} \theta_{mv} \int_0^b \beta_m(\xi) V_m^*(\xi) e^{(x+\rho_{mv})(\xi-b)-\int_\xi^b \mu(\tau)d\tau} d\xi$$

$$+ \eta_{3m} q_2 \rho_{mv} \theta_{mv} \int_0^b \int_0^\xi \beta_m(\eta) V_m^*(\eta) e^{x(\eta-b)+\rho_{mv}(\eta-\xi)+\kappa_{mv}(\xi-b)-\int_\eta^b \mu(\tau)d\tau} d\eta d\xi \Bigg] db$$

$$\times \int_0^\sigma \gamma_m(b) \Bigg[\int_0^b \beta_f(\xi) S_f^*(\xi) e^{(x+\rho_f)(\xi-b)-\int_\xi^b \mu(\tau)d\tau} d\xi$$

$$+ \eta_{1f} p_1 \rho_f \int_0^b \int_0^\xi \beta_f(\eta) S_f^*(\eta) e^{x(\eta-b)+\rho_f(\eta-\xi)+\kappa_f(\xi-b)-\int_\eta^b \mu(\tau)d\tau} d\eta d\xi$$

$$+ \eta_{2f} \theta_{fv} \int_0^b \beta_f(\xi) V_f^*(\xi) e^{(x+\rho_{fv})(\xi-b)-\int_\xi^b \mu(\tau)d\tau} d\xi$$

$$+ \eta_{3f} p_2 \rho_{fv} \theta_{fv} \int_0^b \int_0^\xi \beta_f(\eta) V_f^*(\eta) e^{x(\eta-b)+\rho_{fv}(\eta-\xi)+\kappa_{fv}(\xi-b)-\int_\eta^b \mu(\tau)d\tau} d\eta d\xi \Bigg] db \Bigg\}$$

$$= G(x) = G(Re\lambda^\dagger).$$

Hence, the inequalities $G'(\lambda) < 0$ and $G(\lambda^*) \le G(Re\lambda^\dagger)$ show that $Re\lambda^\dagger \le \lambda^*$. □

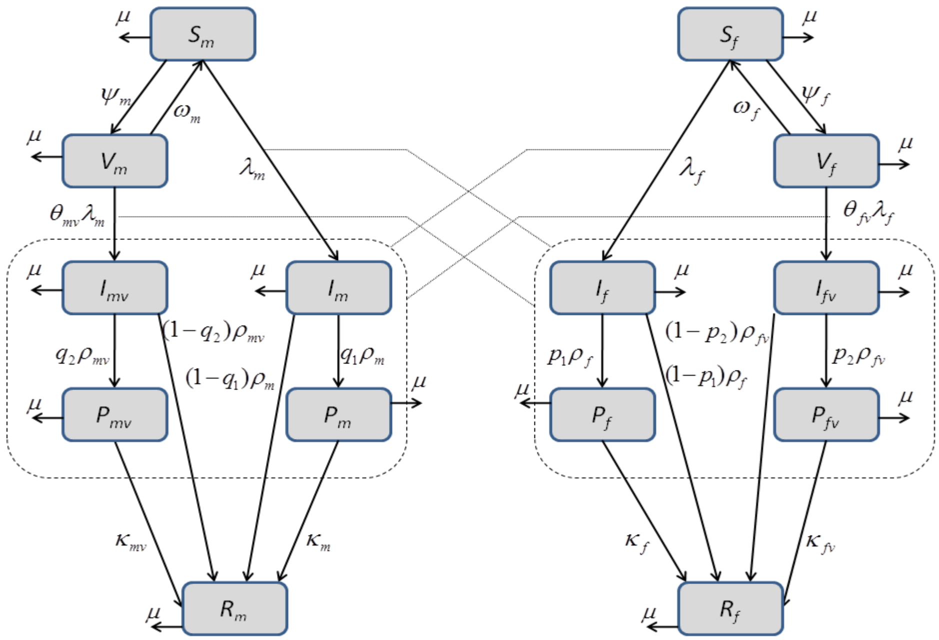

FIGURE 1. Schematic diagram of the model (2).

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