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Understanding the impact of HIV on mpox transmission in the MSM population: A mathematical modeling study

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ABSTRACT

The recent mpox outbreak (in 2022–2023) has different clinical and epidemiological features compared with previous outbreaks of the disease. During this outbreak, sexual contact was believed to be the primary transmission route of the disease. In addition, the community of men having sex with men (MSM) was disproportionately affected by the outbreak. This population is also disproportionately affected by HIV infection. Given that both diseases can be transmitted sexually, the endemicity of HIV, and the high sexual behavior associated with the MSM community, it is essential to understand the effect of the two diseases spreading simultaneously in an MSM population. Particularly, we aim to understand the potential effects of HIV on an mpox outbreak in the MSM population. We develop a mechanistic mathematical model of HIV and mpox co-infection. Our model incorporates the dynamics of both diseases and considers HIV treatment with antiretroviral therapy (ART). In addition, we consider a potential scenario where HIV infection increases susceptibility to mpox, and investigate the potential impact of this mechanism on mpox dynamics. Our analysis shows that HIV can facilitate the spread of mpox in an MSM population, and that HIV treatment with ART may not be sufficient to control the spread of mpox in the population. However, we showed that a moderate use of condoms or reduction in sexual contact in the population combined with ART is beneficial in controlling mpox transmission. Based on our analysis, it is evident that effective control of HIV, specifically through substantial ART use, moderate condom compliance, and reduction in

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sexual contact, is imperative for curtailing the transmission of mpox in an MSM population and mitigating the compounding impact of these intertwined epidemics.

1. Introduction

Mpox (formerly known as monkeypox) is a viral disease caused by the mpox virus, a member of the Orthopoxviridae family. These double-stranded DNA viruses can infect both humans and animals (Elsayed et al., 2022; Saldana et al., 2023). The variola virus, a well-known member of this family and the causative agent of smallpox, was ultimately eradicated in 1980 (Lambo, 1981). Other members of this family of viruses include the vaccinia virus, which can cause a smallpox-like disease in humans, and in a modified form is used in the preparation of smallpox and mpox vaccines (Volz and Sutter, 2017). Mpox is primarily transmitted through close contact with infected animals or individuals (Pan et al., 2023), and is endemic to several countries in West and Central Africa (Ogoina et al., 2020).

In late April–May 2022, a rapid increase in mpox cases in some non-endemic countries outside of Africa led the World Health Organization to declare the outbreak a Global Public Health Emergency on July 23, 2022 (Nuzzo et al., 2022). The United States Department of Health and Human Services declared mpox a Public Health Emergency on August 4, 2022 (Philpott et al., 2022). Unlike the previous outbreaks of mpox, the 2022–2023 outbreak primarily affected cisgender men having sex with men (MSM). Several reports from the USA and Europe suggest that around 40% and up to 90% of cases in some settings occurred in people living with HIV (PWH) (Li et al., 2023; Liu et al., 2023; Thornhill et al., 2022). During the 2022–2023 outbreak, it was evident that mpox was mainly transmitted through close contact, either through sexual activity or body fluids such as saliva and seminal fluid (Adamson et al., 2023). Overall, the majority of the cases during the outbreak were mild and resolved without treatment; however, some severe cases requiring hospitalization and intensive care, and even fatalities, were reported, primarily in immunocompromised individuals, including those with advanced, untreated human immunodeficiency virus (HIV) disease (Chastain et al., 2023).

HIV, which is responsible for causing HIV infection, which, if untreated, progresses to acquired immunodeficiency syndrome (AIDS), continues to pose a significant global public health and socio-economic concern since its emergence in the early 1980s (Tollett et al., 2024; Centers for Disease Control (CDC), 1989). The disease is responsible for 1.5 million new infections and 1 million deaths worldwide each year (Our World in Data). Currently, approximately 39 million individuals are living with HIV/AIDS (Kaiser Family Foundation; U.S. Department of Health & Human Services; UNAIDS), and 40% of new HIV infections are transmitted by individuals unaware of their HIV status (Centers for Disease Control and Preventiona). Several preventive and therapeutic strategies are being implemented to control and mitigate the spread of HIV/AIDS; however, the virus continues to spread worldwide (Centers for Disease Control and Preventionb). Key preventive measures include the promotion of condom use, widespread testing to identify HIV-infected individuals, screening for HIV in pregnant women, public health education, counseling to discourage risky sexual practices leading to HIV transmission, and ensuring access to sterile needles and injecting equipment (Centers for Disease Control and Preventionb; NHS). Additionally, pre-exposure prophylaxis (PrEP), used as a preventive measure, and post-exposure prophylaxis (PEP), taken within 72 h after potential HIV exposure, are also employed. The primary therapeutic approach involves the use of antiretroviral treatment (ART), aiming to reduce the viral load to undetectable levels, thereby keeping the immune system healthy and preventing transmission. However, in the fight against HIV/AIDS, prevention and treatment are not completely separable, but rather interconnected. This is indicated by the concept of "Treatment as Prevention" (TasP), which leverages the efficacy of ART by highlighting that individuals on effective treatment with an undetectable viral load cannot sexually transmit the virus, as encapsulated in the principle "Undetectable equals Untransmittable" (U=U). Finally, in high-income countries, HIV incidence remains elevated among MSM, particularly in large urban settings (CDC, 2012; Surveillance, 2010; Tomas et al., 2015; Toronto Public Health, 2014).

In Canada, the incidence of HIV infection among MSM varies from 0.62 to 1.14% per year, a pattern comparable to the rates observed in other developed countries (MacFadden et al., 2016). As of 2020, an estimated 62,790 individuals were living with HIV in Canada (The epidemiology of HIV in). Furthermore, 90% of PWH (56,200 individuals) had received an official diagnosis, and 87% of those diagnosed (48,660 individuals) were receiving HIV treatment. Notably, 95% of those undergoing treatment had achieved viral suppression (46,100 U=U individuals) (The epidemiology of HIV in). In addition, it is estimated that 33,335 gay, bisexual, and other MSM (gbMSM) were living with HIV in Canada in 2020. This represents 53.1% of all the PWH residing in Canada. The overall estimate of PWH also included 31,589 MSM who did not self-identify as gbMSM and 1746 MSM who injected drugs (PWID) (The epidemiology of HIV in). Of note, 96% of gbMSM diagnosed with HIV were on HIV treatment. Despite the scale-up of joint ART and consistent investments in behavioral prevention programs, (Furler et al., 2006), the rates of newly diagnosed HIV infections and HIV-related deaths within the MSM population in Canada have not significantly decreased over the past decade, still representing a significant public health concern (MacFadden et al., 2016).

PWH have been adversely affected by the 2022–2023 mpox outbreak, accounting for about 40% of diagnosed mpox cases (Barboza et al., 2023; Mitjà et al., 2023a; Mitjà et al., 2023b; Ortiz-Saavedra et al., 2023; Multi-Country Outbreak of Mpox).

PWH are more vulnerable to certain infections, including mpox, because of their weakened immune systems (CDC health advisory). However, even though it is reasonable to assume that, because of underlying immunosuppression, the course of mpox can be more severe in PWH, the effects of mpox in this patient population have yet to be determined (Farahat et al.). The working hypothesis according to which HIV may enhance mpox virus transmission and *vice versa* had already been formulated before the 2022–2023 mpox outbreak (Ogoina et al., 2020). For instance, Alakunle et al. (Alakunle et al., 2020) reported that the transmissibility of mpox could be higher in PWH (Alakunle et al., 2020). On the other hand, the high prevalence of mpox and HIV co-infection (40%) could just be due to the fact that most of the cases occurred in the MSM community and that MSM have a greater HIV prevalence than the general population (Comparison of the Prevalence Rates, 2019; Curran et al., 2022). Also, HIV-positive patients are more likely to attend a health care facility and have a diagnostic test for mpox compared to HIV-negative patients (Ghaffar et al., 2022). Although there is currently no strong evidence to support the use of antiviral drugs directed against mpox (Kuroda et al., 2023; Ortiz-Saavedra et al., 2022), such as tecovirimat or cidofovir, the CDC's "Interim Guidance for Prevention and Treatment of mpox in Persons with HIV Infection" (O'Shea et al., 2022) recommends the use of tecovirimat according to the viral and immunological status of the patient to avoid possible complications (Kuehn, 2022).

Mathematical modeling plays a key role in monitoring, controlling, and forecasting infectious disease outbreaks (Siettos and Russo, 2013), providing significant support to public health decision- and policy-makers in the design and implementation of control measures. Mathematical models have also been devised to study, track, and predict the dynamics of STIs and assess the effectiveness of packages of public health interventions (Ferguson and Garnett, 2000). In the last years, some mathematical models have been developed to study the transmission dynamics of mpox (Bisanzio and Reithinger, 2022; Bragazzi et al., 2022; Endo et al., 2022; Luigi Bragazzi et al., 2023; NO et al., 2020; Peter et al., 2021; Usman Isa Adamu et al., 2017; Vibhaav Bankuru et al., 2020; Yuan et al., 2022). Models to understand the co-interaction of mpox with other diseases have also been investigated (Bhunu et al., 2012; Ifeanyi Marcus et al., 2024; Odiba Peace et al., 2024; Zhang et al., 2023). In particular, Bhunu et al. (Bhunu et al., 2012) investigated the co-dynamics of HIV and mpox before the 2022–2023 outbreak, where they carried out bifurcation and global stability analysis and also assessed the impact of animal spread on the dynamics of both diseases. Their results showed that HIV enhances mpox infection and *vice versa*. Marcus et al. (Ifeanyi Marcus et al., 2024) carried out sensitivity and bifurcation analyses of an mpox-HIV co-infection model. They showed that the mpox and HIV submodels could undergo a forward bifurcation under certain conditions. A compartmental model to examine the co-interaction between mpox, COVID-19 and HIV was designed and analyzed by Peace et al. (Odiba Peace et al., 2024). Although the study did not investigate the impact of HIV on mpox transmission, the authors proposed different intervention measures for controlling the co-circulation of the three diseases within a given population. In general, many of the aforementioned studies on mpox or its co-infection with other diseases were carried out before the 2022–2023 mpox outbreak, or, if conducted during the outbreak, did not focus on the combined effects of HIV infection, its treatment, and reduction in sexual activity on the mpox epidemic in an MSM population. Therefore, the present study was undertaken to fill in this research gap in the currently available body of scholarly knowledge.

The rest of the paper is structured as follows: In Section 2, we present the mathematical model formulation and derivation. Important features of the mpox and HIV submodels, as well the invasion reproduction number and its interpretation are presented in Section 3. Sensitivity analysis on the reproduction numbers and epidemic peak size/time are presented in Section 4. Scenario analysis on the mpox invasion reproduction number are presented in Section 5. Model simulations are carried out in Section 6 while detailed discussion and concluding remarks are given in Section 7.

2. Mathematical model formulation and derivation

We develop a mechanistic mathematical model to study HIV and mpox co-infection. Our study focuses on the MSM community since this population was disproportionately affected by the most recent outbreak of mpox around the world (Ortiz-Saavedra et al., 2023) and also because they are at a high-risk of both HIV and mpox.

With different disease progression stages, our model has 12 compartments: susceptible (S) (contains individuals susceptible to both diseases), mpox-exposed (E_m), mpox-infectious (I_m), mpox-recovered (R_m), HIV-infected (I_h), HIV-infected and mpox-exposed (E_{hm}), HIV-infected and mpox-infectious (I_{hm}), HIV-infected and mpox-recovered (R_{hm}), HIV-infected on ART (I_h^T), HIV-infected on ART and mpox-exposed (E_{hm}^T), HIV-infected on ART and mpox-infectious (I_{hm}^T), and HIV-infected on ART and mpox-recovered (R_{hm}^T) (see Fig. 1).

Although individuals at the exposed stage of mpox are infected, they are not infectious and cannot transmit the virus to others (World Health Organization). We assume mpox transmission happens only at the infectious stage through sexual contact. Our model does not consider the individuals who became infected with HIV while they were exposed, infectious, or who have recovered from mpox, as this is not the focus of this study. In addition, the HIV incubation period may be higher than the time course of mpox infection in these individuals and as a result, they may not be aware of the HIV infection throughout their mpox infection (Centers for Disease Control and Preventionc; Leo, 1995; Konrad et al., 2017). For a similar reason, we do not consider the exposed stage of HIV. An HIV-infected individual not on ART may start ART at any time while infected with mpox. However, we assume that those at the infectious stage of mpox are more likely to resume ART as they may seek medical attention during this period. Even though mpox reinfection has been reported (Golden et al., 2023; Hazra et al., 2023; Musumeci et al., 2023; The Lancet Infectious Diseases, 2023), its occurrence within our study period is unlikely. As

a result, we omit reinfection in our model. Since we are interested in the mpox infections that happen within the MSM population, the recruitment into the susceptible compartment (S) refers to the recruitment of new individuals into the MSM population only. On the other hand, individuals can exit the MSM community from any compartment of the model. We assume that death due to mpox can only occur at the infectious stage of the disease (i.e., in the I_m, I_{hm}, and I_{hm}^T compartments) and death due to HIV can occur among all HIV-infected individuals, regardless of their mpox status. However, we assume that HIV-related deaths are lower among those on ART. The model equations are:

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - (\lambda_m + \lambda_h)S - \mu S,\\
\frac{dE_m}{dt} &= \lambda_m S - (\alpha + \mu)E_m,\\
\frac{dI_m}{dt} &= \alpha E_m - (\gamma + \mu + \delta_m)I_m,\\
\frac{dR_m}{dt} &= \gamma I_m - \mu R_m,\\
\frac{dI_h}{dt} &= \lambda_h S - \lambda_{hm} I_h - (\tau + \delta_h + \mu)I_h,\\
\frac{dI_h^T}{dt} &= \tau I_h - \lambda_{hm}^T I_h^T - \left(\delta_h^T + \mu\right)I_h^T,\\
\frac{dE_{hm}}{dt} &= \lambda_{hm} I_h - (\tau + \alpha + \delta_h + \mu)E_{hm},\\
\frac{dI_{hm}}{dt} &= \alpha E_{hm} - (\gamma + \rho\,\tau + \delta_{hm} + \mu)I_{hm},\\
\frac{dR_{hm}}{dt} &= \gamma I_{hm} - (\tau + \delta_h + \mu)\,R_{hm},\\
\frac{dE_{hm}^T}{dt} &= \lambda_{hm}^T\, I_h^T + \tau E_{hm} - \left(\alpha + \delta_h^T + \mu\right)E_{hm}^T,\\
\frac{dI_{hm}^T}{dt} &= \alpha E_{hm}^T + \rho\,\tau I_{hm} - \left(\gamma + \delta_{hm}^T + \mu\right)I_{hm}^T,\\
\frac{dR_{hm}^T}{dt} &= \gamma I_{hm}^T + \tau\, R_{hm} - (\delta_h^T + \mu)\,R_{hm}^T,
\end{aligned} \tag{2.1}$$

where α is the transition rate from the exposed to the infectious stage of mpox, γ is the mpox recovery rate, δ_m and δ_h are the death rates due to mpox and HIV, respectively, and δ_{hm} is the death rate due to HIV or mpox for co-infected individuals. For the HIV-infected individuals on ART, the death rate due to HIV is δ_h^T, and the death rate due to either HIV or mpox for those that are co-infected is δ_{hm}^T. We assume that HIV-infected individuals who are not on ART, but exposed or who have recovered from mpox seek HIV treatment at the same rate (τ) as those who have not contracted mpox infection. However, those who are mpox-infectious may be put on HIV treatment at a relatively higher rate $\rho\tau$, where $\rho > 1$, since they are more likely to seek medical attention due to the mpox infection. The description of the state variables are provided in Table 1.

Since we are considering the MSM population only, we define Λ as the entry rate into this population, and μ as the exit rate from the population, which may be due to natural death or emigration. The forces of infection for mpox (λ_m) and HIV (λ_h) transmissions are given by:

$$\lambda_m = \frac{c\,p_m(1-\nu\epsilon)(I_m + I_{hm} + I_{hm}^T)}{N}; \tag{2.2a}$$

$$\lambda_h = \frac{c\,p_h(1-\nu\epsilon)\left[I_h + E_{hm} + I_{hm} + R_{hm} + \eta\left(I_h^T + E_{hm}^T + I_{hm}^T + R_{hm}^T\right)\right]}{N}, \tag{2.2b}$$

where $p_m(p_h)$ is the mpox (HIV) transmission probability per contact, and c is the average per-capita sexual contact per day. We define the mpox transmission rate (β_m) as the product $c\,p_m$ and the transmission rate of HIV (β_h) as the product $c\,p_h$. We incorporate the effect of interventions, such as condom use, into our model through the forces of infection (λ_m and λ_h) by scaling the transmission probabilities p_m and p_h, where $0 \le \nu \le 1$ is the condom use compliance rate and $0 < \varepsilon < 1$ is the effectiveness of condoms in preventing both mpox and HIV infections. In this formulation, we define the condom-related preventability level (ξ) as the product $\nu\varepsilon$, with $0 \le \nu\varepsilon < 1$. Also, $\nu = 0$ implies that no compliance to condom usage at all while $\nu = 1$ means 100% compliance to condom usage. ε very near zero means very low condom efficacy while ε very near 1

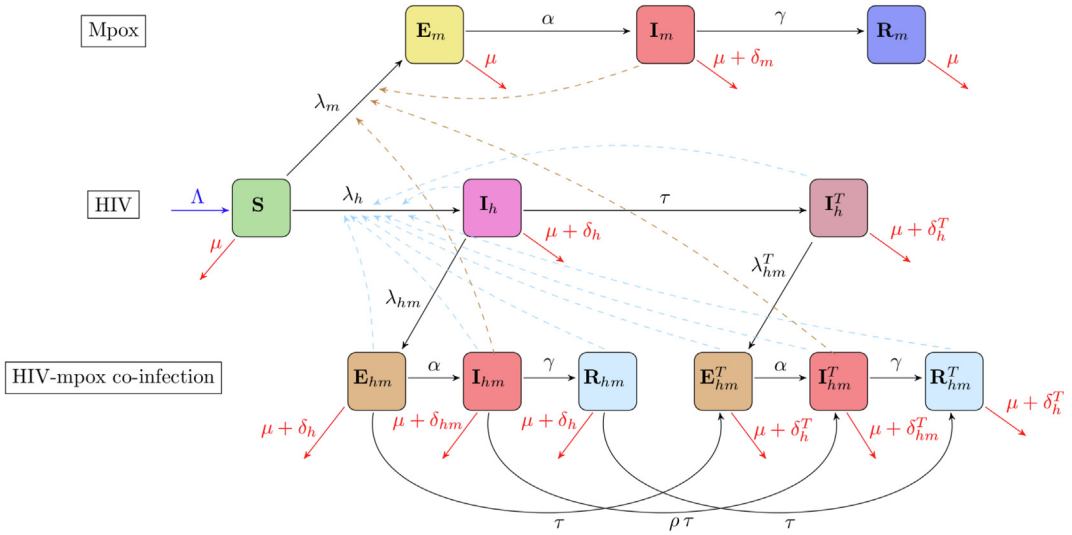


Fig. 1. Schematic illustration of the HIV-mpox co-infection model. The population is stratified into three main groups: i) mpox-infected individuals, ii) HIV-infected individuals, and iii) HIV-mpox co-infected individuals. The model compartments are: susceptible (S), mpox-exposed (E_m), mpox-infectious (I_m), mpox-recovered (R_m), HIV-infected (I_h), HIV-infected and mpox-exposed (E_{hm}), HIV-infected and mpox-infectious (I_{hm}), HIV-infected and mpox-recovered (R_{hm}), HIV-infected on ART (I_h^T), HIV-infected on ART and mpox-exposed (E_{hm}^T), HIV-infected on ART and mpox-infectious (I_{hm}^T), and HIV-infected on ART and mpox-recovered (R_{hm}^T). Black solid arrows show the transition of individuals through the different stages of the diseases at the rates indicated close to the arrows, red solid arrows indicate exit from the MSM population (due to death or emigration). Blue solid arrow shows entry into the MSM population. Blue and brown dashed arrows indicate HIV and mpox transmission, respectively (see (2.1) for more details).

Table 1
Description of model variables.

Variable	Description
S	Susceptible individuals
E_m	Mpox-exposed individuals
I_m	Mpox-infectious individuals
R_m	Mpox-recovered individuals
I_h	HIV-infected individuals
E_{hm}	HIV-infected and mpox-exposed individuals
I_{hm}	HIV-infected and mpox-infectious individuals
R_{hm}	HIV-infected and mpox-recovered
I_h^T	HIV-infected individuals on anti-retroviral therapy (ART)
E_{hm}^T	HIV-infected individuals on ART and mpox-exposed
I_{hm}^T	HIV-infected individuals on ART and mpox-infectious
R_{hm}^T	HIV-infected on ART and mpox-recovered

implies very high condom efficacy. We also assume that ART reduces HIV infectiousness (Cohen et al., 2011; Eisinger et al., 2019) and we incorporate this effect into the force of infection λ_h using the parameter $0 \leq \eta \leq 1$.

Furthermore, we consider the possibility that HIV infection increases susceptibility to mpox infection (CDC health advisory), and that HIV-infected individuals who are not on ART are more susceptible to mpox, compared with those who are on ART (Centers for disease control and prevention). This effect is incorporated into our model by scaling the mpox force of infection (λ_m) to obtain $\lambda_{hm} = \sigma\lambda_m$ for HIV-infected individuals not on ART and $\lambda_{hm}^T = \sigma^T\lambda_m$ for those who are on ART, where $\sigma > 1$ and $\sigma^T > 1$ are scaling parameters used to model the increase in susceptibility, with $\sigma > \sigma^T$.

3. Reproduction numbers

In this section, we present some important features of the co-infection model (2.1), an mpox sub-model, and a HIV sub-model. We compute the control reproduction numbers of these models using the next-generation matrix approach (Van den Driessche and Watmough, 2002) and discuss their biological interpretations. Detailed computation of the reproduction numbers is provided in Appendix A.

3.1. Mpox sub-model

We start by considering the mpox sub-model. The mpox sub-model is obtained from the co-infection model (2.1) by setting the variables related to HIV and co-infection dynamics ($I_h, I_h^T, E_{hm}, I_{hm}, R_{hm}, E_{hm}^T, I_{hm}^T$, and R_{hm}^T) to zero. The model is applicable to a scenario where only mpox is introduced and spread through a population. Its equations are given by

$$\begin{aligned}
\frac{\mathrm{d}S}{\mathrm{d}t} &= \Lambda - \lambda_{ms} S - \mu S,\\
\frac{\mathrm{d}E_m}{\mathrm{d}t} &= \lambda_{ms} S - (\alpha + \mu) E_m,\\
\frac{\mathrm{d}I_m}{\mathrm{d}t} &= \alpha E_m - (\gamma + \delta_m + \mu) I_m,\\
\frac{\mathrm{d}R_m}{\mathrm{d}t} &= \gamma I_m - \mu R_m,
\end{aligned} \tag{3.1}$$

where λ_{ms} is the force of infection, given by

$$\lambda_{ms} = \frac{c\, p_m (1 - \nu\epsilon) I_m}{S + E_m + I_m + R_m}.$$

The control reproduction number for the mpox sub-system is given by (see Appendix A.1 for derivation):

$$\mathcal{R}_c^m = \frac{c\, p_m (1 - \nu\epsilon)\, \alpha}{(\alpha + \mu)(\gamma + \delta_m + \mu)}.$$

This is the average number of secondary mpox infections caused by one infectious individual in a population completely susceptible to mpox without HIV.

3.2. HIV sub-model

Next, we consider the HIV sub-model. The HIV sub-model is obtained from the co-infection model (2.1) by setting the variables related to mpox and co-infection dynamics ($E_m, I_m, R_m, E_{hm}, I_{hm}, R_{hm}, E_{hm}^T, I_{hm}^T$, and R_{hm}^T) to zero. This model describes the dynamics of HIV in the population when there is no mpox. Its equations are

$$\begin{aligned}
\frac{\mathrm{d}S}{\mathrm{d}t} &= \Lambda - \lambda_{hs} S - \mu S,\\
\frac{\mathrm{d}I_h}{\mathrm{d}t} &= \lambda_{hs} S - (\tau + \delta_h + \mu) I_h,\\
\frac{\mathrm{d}I_h^T}{\mathrm{d}t} &= \tau I_h - \left(\delta_h^T + \mu\right) I_h^T,
\end{aligned} \tag{3.2}$$

where λ_{hs} is the force of infection for this model given by

$$\lambda_{hs} = \frac{c\, p_h (1 - \nu\epsilon)(I_h + \eta I_h^T)}{S + I_h + I_h^T}.$$

The control reproduction number for the HIV sub-model is given by (see Appendix A.2 for derivation):

$$\mathcal{R}_c^h = \frac{c\, p_h (1 - \nu\epsilon)}{(\tau + \delta_h + \mu)} + \frac{\eta\, c\, p_h (1 - \nu\epsilon)\tau}{(\tau + \delta_h + \mu)(\delta_h^T + \mu)}. \tag{3.3}$$

The first term in the expression for $\mathcal{R}_c^h$ in (3.3) represents the contribution of the untreated HIV-infected individuals to the spread of the disease, while the second term accounts for the contributions of those on ART. Observe that this contribution vanishes if ART is 100% effective in preventing infectiousness or transmission ($\eta = 0$). Overall, as expected, $\mathcal{R}_c^h = 0$ when condom use is 100% effective in preventing infection (i.e., $\nu\varepsilon = 1$).

The endemic equilibrium of the HIV sub-model (3.2) is defined by

$$\Psi_{eh} = \left(S^*, I_h^*, I_h^{T*}\right),$$

where the steady states S^*, I_h^*, and I_h^{T*} are given by

$$S^* = \frac{\Lambda(\delta_h^T + \mu + \tau)}{\Upsilon\left(\mathcal{R}_c^h - 1\right) + \chi}, \qquad I_h^* = \frac{\Lambda(\delta_h^T + \mu)\left(\mathcal{R}_c^h - 1\right)}{\Upsilon\left(\mathcal{R}_c^h - 1\right) + \chi}, \qquad I_h^{T*} = \frac{\Lambda\tau\left(\mathcal{R}_c^h - 1\right)}{\Upsilon\left(\mathcal{R}_c^h - 1\right) + \chi}, \tag{3.4}$$

where $\Upsilon = (\tau + \delta_h + \mu)(\delta_h^T + \mu)$ and $\chi = \mu(\delta_h^T + \mu + \tau)$. Here, $\mathcal{R}_c^h$ is the control reproduction number for the HIV sub-model, defined in (3.3).

3.3. HIV-mpox co-infection model

Lastly, we consider the HIV-mpox co-infection model (2.1) and use the model to compute an invasion reproduction number for mpox. The invasion reproduction number is computed around the HIV endemic equilibrium given by

$$\Psi_{eh} = \left(S^*, 0, 0, 0, I_h^*, I_h^{T*}, 0, 0, 0, 0, 0, 0\right),$$

Using the next-generation matrix method (Van den Driessche and Watmough, 2002), we obtain (see Appendix A.3 for details)

Table 2
Description of model parameters. $CN_{pop} = 38,929,902$ is the total population of Canada at the beginning of the 2022–2023 mpox outbreak in Canada (Population and total).

Parameter	Description	Value	Source
p_m	Mpox transmission probability per contact	0.1–0.9	(Adam et al., 2023; Beer and Rao, 2019; Luigi Bragazzi et al., 2023; Miura et al., 2022; Spicknall et al., 2022)
c	Average per capita sexual contact per unit time	$\frac{1}{365} - 2.0\ \text{day}^{-1}$	Luigi Bragazzi et al. (2023)
p_h	HIV transmission probability per contact	$0.0011 - 0.039$	(Lima et al., 2021; Tollett et al., 2024)
ν	Condom compliance rate	Varied	–
ε	Condom efficacy	0.92	Mukandavire et al. (2007)
ξ	Condom preventability level	$\nu\varepsilon$	–
μ	Exit rate from the MSM population	$0.00012 - 0.0043\ \text{day}^{-1}$	MacFadden et al. (2016)
N	Total population	4% of CN_{pop}	(Population and total)
Λ	Recruitment rate into the MSM population	$N \times \mu\ \text{day}^{-1}$	(MacFadden et al., 2016; Population and total)
γ	Mpox recovery rate	$\frac{1}{28} - \frac{1}{14}\ \text{day}^{-1}$	(World Health Organization; Adam et al., 2023)
α	Progression rate to symptomatic stage of mpox	$\frac{1}{8.5}\ \text{day}^{-1}$	(World Health Organization; Centers for Disease Control and Preventiond)
τ	Rate of enrolment on HIV treatment or ART	0.0015–0.035	(Lima et al., 2021; Tollett et al., 2024)
ρ	Scaling parameter for increased rate of ART enrollment for co-infected individuals	1.2	Assumed
δ_m	Mpox-induced death rate	0	(Government of Canada)
δ_h	HIV induced death rate among individuals not enrolled on ART	$0.000035 - 0.0095\ \text{day}^{-1}$	Lima et al. (2021)
δ_{hm}	Disease induced death rate among co-infected individuals not enrolled on ART	$0.000035 - 0.0095\ \text{day}^{-1}$	Lima et al. (2021)
δ_h^T	HIV induced death rate among individuals enrolled on ART	$0\ \text{day}^{-1}$	Lima et al. (2021)
δ_{hm}^T	Disease induced death rate among co-infected individuals enrolled on ART	$0\ \text{day}^{-1}$	Lima et al. (2021)
σ	Scaling parameter for increased susceptibility to mpox due to HIV infection	1.5	(CDC health advisory)
σ^T	Scaling parameter for increased susceptibility to mpox due to HIV infection for individuals enrolled on ART	1.3	(Centers for disease control and prevention)
η	Scaling parameter for reduced infectiousness of individuals enrolled on ART	$0 - 1$	Lima et al. (2021)
$\Omega = \frac{I_h^T}{I_h + I_h^T}$	Proportion of HIV-infected individuals on ART at the beginning of mpox oubreak	$0 - 1$	

$$\mathcal{R}_c^{mh} = \mathcal{R}_{c,1}^{mh} + \mathcal{R}_{c,2}^{mh} + \mathcal{R}_{c,3}^{mh}, \tag{3.5a}$$

where

$$\mathcal{R}_{c,1}^{mh} = \frac{c\,p_m(1-\nu\epsilon)\alpha S^*}{(\alpha+\mu)(\gamma+\delta_m+\mu)N^*}, \tag{3.5b}$$

$$\mathcal{R}_{c,2}^{mh} = \frac{\sigma c\,\alpha\,p_m(1-\nu\epsilon)I_h^*}{(\tau+\alpha+\delta_h+\mu)N^*}\left[\frac{1}{\Phi}+\frac{\rho\tau}{\Phi\,(\gamma+\delta_{hm}^T+\mu)}+\frac{\tau}{(\alpha+\delta_h^T+\mu)(\gamma+\delta_{hm}^T+\mu)}\right], \tag{3.5c}$$

$$\mathcal{R}_{c,3}^{mh} = \frac{\sigma^T c\,p_m(1-\nu\epsilon)\alpha I_h^{T*}}{(\alpha+\delta_h^T+\mu)(\gamma+\delta_{hm}^T+\mu)N^*}. \tag{3.5d}$$

Here, $\Phi = \gamma + \rho\tau + \delta_{hm} + \mu$ and N^* is the total population at mpox-free and HIV endemic equilibrium, given by

$$N^* = \frac{\Lambda\left[\left(\delta_h^T+\mu+\tau\right)+(\delta_h^T+\mu)\left(\mathcal{R}_c^h-1\right)+\tau\left(\mathcal{R}_c^h-1\right)\right]}{(\tau+\delta_h+\mu)(\delta_h^T+\mu)\left(\mathcal{R}_c^h-1\right)+\mu(\delta_h^T+\mu+\tau)},$$

where $\mathcal{R}_c^h$ is the control reproduction number for the HIV sub-model given in (3.3), which is greater than one at the HIV endemic equilibrium.

The invasion reproduction number shows the average number of secondary infections with one disease generated by a single infectious individual in a population that is endemic for another disease. For our co-infection model, the mpox invasion reproduction number (3.5) gives the average number of secondary mpox infections generated by a single infectious individual in a population that is endemic for HIV. It has three terms, where the first term $\mathcal{R}_{c,1}^{mh}$ corresponds to the average secondary mpox infections coming from the completely susceptible population. The second term $\mathcal{R}_{c,2}^{mh}$ represents the average secondary mpox infections coming from the HIV-infected population not on ART. Lastly, the third term $\mathcal{R}_{c,3}^{mh}$ accounts for the average secondary mpox infections coming from the HIV-infected population on ART. Detailed biological interpretation of each term in the mpox invasion reproduction number (3.5) is given in Table 3. Also, an equivalent expression of the mpox invasion reproduction number written in terms of the proportion of HIV-infected individuals on ART at the beginning of mpox outbreak (Ω) is given in Appendix A.3.

Table 3
Interpretation of the terms in the mpox invasion reproduction number $\mathcal{R}_c^{mh}$ in Eq. (3.5).

Term	Interpretation
$\frac{c\,p_m(1-\nu\epsilon)\alpha S^*}{(\alpha+\mu)(\gamma+\delta_m+\mu)N^*}$	The average number of secondary mpox infections caused by one initial susceptible individual who acquires mpox and becomes exposed and progresses to the infectious stage without contracting HIV ($S_h \to E_m \to I_m$), during mpox infectious period, in the susceptible population at HIV endemic equilibrium.
$\frac{c\,p_m(1-\nu\epsilon)\sigma\alpha I_h^*}{(\tau+\alpha+\delta_h+\mu)(\gamma+\rho\tau+\delta_{hm}+\mu)N^*}$	The average number of secondary mpox infections caused by one initial untreated HIV-infected individual who is then co-infected with mpox going through the route $I_h \to E_{hm} \to I_{hm}$, during mpox infectious period, in the untreated HIV-infected population at HIV endemic equilibrium.
$\frac{c\,p_m(1-\nu\epsilon)\sigma\alpha\rho\tau I_h^*}{(\tau+\alpha+\delta_h+\mu)(\gamma+\rho\tau+\delta_{hm}+\mu)(\gamma+\delta_{hm}^T+\mu)N^*}$	The average number of secondary mpox infections caused by one initial untreated HIV-infected individual who is then co-infected with mpox going through the route $I_h \to E_{hm} \to I_{hm} \to I_{hm}^T$, during mpox infectious period, in the untreated HIV-infected population at HIV endemic equilibrium.
$\frac{c\,p_m(1-\nu\epsilon)\sigma\alpha\tau I_h^*}{(\tau+\alpha+\delta_h+\mu)(\alpha+\delta_h^T+\mu)(\gamma+\delta_{hm}^T+\mu)N^*}$	The average number of secondary mpox infections caused by one initial untreated HIV-infected individual who is then co-infected with mpox going through the route $I_h \to E_{hm} \to E_{hm}^T \to I_{hm}^T$, during mpox infectious period, in the untreated HIV-infected population at HIV endemic equilibrium.
$\frac{c\,p_m(1-\nu\epsilon)\sigma^T\alpha I_h^{T*}}{(\alpha+\delta_h^T+\mu)(\gamma+\delta_{hm}^T+\mu)N^*}$	The average number of secondary mpox infections caused by one initial treated HIV-infected individual who is then co-infected with mpox ($I_h^T \to I_{hm}^T$), during mpox infectious period, in the treated HIV-infected population at HIV endemic equilibrium.

4. Sensitivity analysis

We investigate the sensitivity of the dynamics of the co-infection model (2.1) to the model parameters. The Latin Hypercube Sampling (LHS), introduced by Blower and Dowlatabadi (Blower and Dowlatabadi, 1994) is used to sample model parameters from distributions specified in Table 4. In this analysis, we calculate the Partial Rank Correlation Coefficient (PRCC) for each parameter. The PRCC values range from -1 to 1. Positive (negative) values of PRCC indicate a positive (negative) correlation, while the magnitude reflects the measure of sensitivity. For instance, a magnitude close to zero implies a very minimal impact, whereas a magnitude close to one indicates a very significant impact.

4.1. Sensitivity analysis on reproduction numbers

Our sensitivity analysis on mpox control reproduction number ($\mathcal{R}_c^m$) and mpox invasion reproduction number ($\mathcal{R}_c^{mh}$) (Fig. 2) show that both quantities are sensitive to the contact rate c, mpox transmission probability p_m, and condom preventability level, ξ. Also, both are positively sensitive to the contact rate and transmission probability. In order words, an increase in the contact rate and transmission probability of mpox will increase both $\mathcal{R}_c^m$ and $\mathcal{R}_c^{mh}$. Also, the condom preventability level is negatively correlated with respect to both the mpox control and invasion reproduction numbers. Moreover, we observe that both the mpox control reproduction number ($\mathcal{R}_c^m$) and mpox invasion reproduction number ($\mathcal{R}_c^{mh}$) are most sensitive to condom preventability level, ξ, compared to all other parameters.

Thus, increasing this parameter will reduce $\mathcal{R}_c^m$ and $\mathcal{R}_c^{mh}$. Additionally, other parameters that are negatively correlated with respect to the mpox invasion reproduction number are the scaling parameter for increased rate of enrollment on ART for co-infected individuals (ρ) and the proportion of HIV-infected individuals on ART at the onset of mpox outbreak (Ω). Therefore, increasing these two parameters will reduce the burden of mpox. These results show that an effective control of HIV, specifically through substantial ART use, can help reduce the spread of mpox. Other parameters that are positively correlated with respect to the mpox invasion reproduction number are the scaling parameter for reduced infectiousness of individuals living with HIV who are on ART (η), the scaling parameter for increased susceptibility to mpox by HIV-infected not on ART (σ), and the scaling parameter for increased susceptibility to mpox by individuals on ART (σ^T). An increase in any of these parameters will increase the mpox invasion reproduction number.

4.2. Sensitivity analysis on peak size and time

The sensitivity analysis on the first peak size for the total population of individuals infected with mpox ($I_m + I_{hm} + I_{hm}^T$), presented in Fig. 3(a) reveals that the sexual contact rate (c), the mpox transmission probability (p_m), the scaling parameter for reduced infectiousness of individuals living with HIV who are on ART (η), the scaling parameter for increased susceptibility to mpox by HIV-infected individuals not on ART (σ), and the scaling parameter for increased susceptibility for those on ART (σ^T) are all positively correlated to the peak size for the total population of individuals infected with mpox. Thus, an increase in these quantities will lead to an increase in the peak size for total population of individuals infected with mpox. Conversely, it can also be observed from this figure that the condom preventability level (ξ), the proportion of HIV-infected individuals on ART before mpox outbreak starts (Ω), and the scaling parameter for increased rate of enrollment on ART for co-infected individuals (ρ) are all negatively correlated to the peak size. Observe that the sexual contact rate, mpox transmission probability, condom preventability level, and the scaling parameter for increased susceptibility to mpox by HIV-infected individuals not on ART are more sensitive to the peak size than other model parameters (Fig. 3(a)).

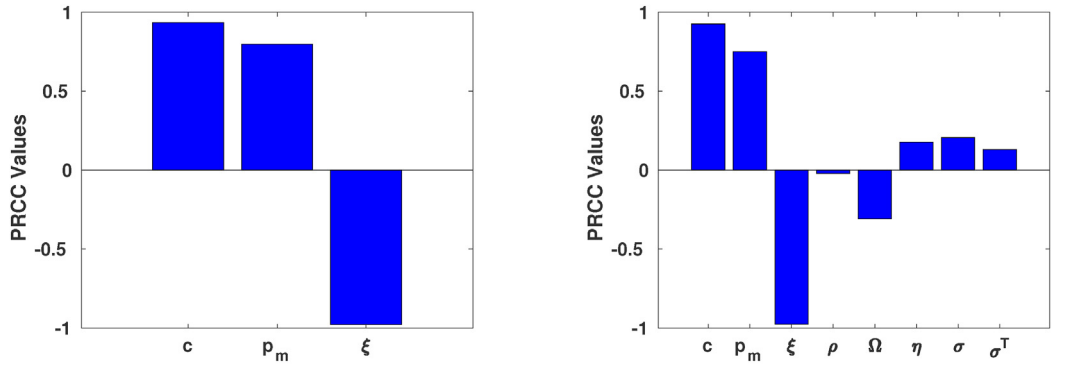
In Fig. 3(b), we present the results for the sensitivity analysis for the timing of the first peak for the total population of individuals infected with mpox. These results show that the peak time is positively sensitive to the condom preventability level (ξ), scaling parameter for increased rate of ART enrollment for co-infected individuals (ρ) and the proportion of HIV-infected individuals on ART before mpox outbreak (Ω). On the other hand, the negatively correlated parameters to the peak time are: the sexual contact rate (c), mpox transmission probability (p_m), scaling parameter for reduced infectiousness of individuals living with HIV who are on ART (η), scaling parameter for increased susceptibility to mpox by HIV-infected individuals not on ART (σ) and the scaling parameter for increased susceptibility to mpox by HIV-infected individuals on ART (σ^T). Note that the magnitude of the peak size sensitivity to the model parameters is relatively consistent with that of the peak time sensitivity for the parameters. In other words, an increase in a model parameter will have opposing influence on the peak size and peak time.

5. Scenario analysis

Next, we perform scenario analysis on the mpox invasion reproduction number with respect to key parameters in the co-infection model. These parameters include the condom preventability level (ξ), the sexual contact rate (c), the proportion of HIV-infected individuals on ART at the beginning of mpox outbreak (Ω), the scaling parameter for increased susceptibility to mpox by HIV-infected individuals not on ART (σ), and the scaling parameter for increased susceptibility to mpox by HIV-infected individuals on ART (σ^T).

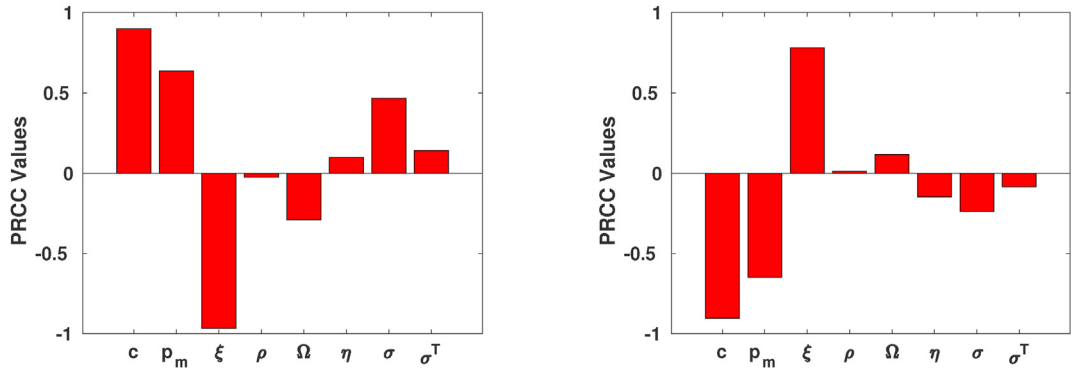
Table 4
Parameter distributions used in sensitivity analysis. T indicates a triangular distribution, with a peak at the fixed value from Table 2. U indicates a uniform distribution.

Parameter	Lower bound	Upper bound	Distribution	Source
C	$\frac{1}{365}$	2.0	T	Luigi Bragazzi et al. (2023)
p_m	0.1	0.9	U	(Adam et al., 2023; Beer and Rao, 2019; Miura et al., 2022)
p_h	0.0011	0.039	U	(Lima et al., 2021; Tollett et al., 2024)
Ξ	0	1.0	T	Mukandavire et al. (2007)
Ω	0	1.0	U	Assumed
P	1.0	2.0	U	Assumed
Σ	1.0	1.8	U	(CDC health advisory)
σ^T	1.0	1.5	T	(Centers for disease control and prevention)
H	0	1.0	T	Lima et al. (2021)



(a) Mpox control reproduction number ($\mathcal{R}_c^m$). (b) Mpox invasion reproduction number ($\mathcal{R}_c^{mh}$).

Fig. 2. Sensitivity analysis on reproduction numbers. Sensitivity of the control reproduction number ($\mathcal{R}_c^m$) (a) and invasion reproduction number ($\mathcal{R}_c^{mh}$) (b) to the model parameters. Positive (negative) values of PRCC indicate a positive (negative) correlation between the quantities and the corresponding model parameter, while the magnitude reflects the measure of sensitivity.



(a) Sensitivity analysis on peak size. (b) Sensitivity analysis on peak time.

Fig. 3. Sensitivity analysis on the total population of individuals infected with mpox. Sensitivity analysis on the first peak size (a) and time (b) for the total population of individuals infected with mpox ($I_m + I_{hm} + I_{hm}^T$). Positive (negative) values of PRCC indicate a positive (negative) correlation between the quantities and the corresponding model parameter, while the magnitude reflects the measure of sensitivity.

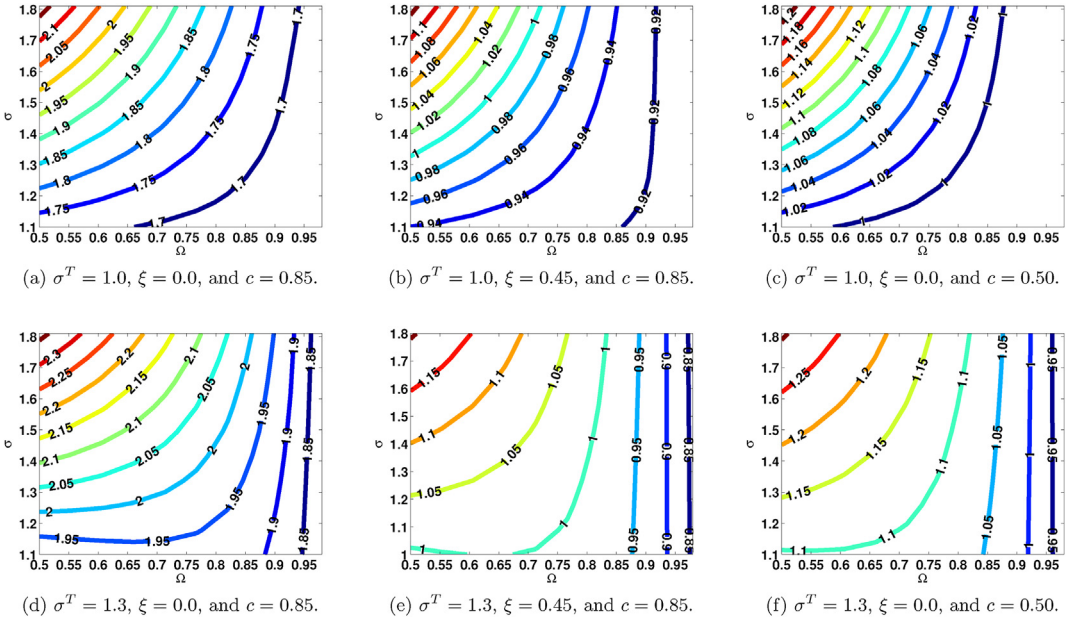
The effect of the proportion of HIV-infected individuals on ART before the invasion of mpox Ω and the scaling parameter for increased susceptibility to mpox for HIV-infected individuals not on ART σ, on the mpox invasion reproduction number ($\mathcal{R}_c^{mh}$) is presented in Fig. 4. In the top panel, we show the results for when HIV infection does not increase susceptibility to mpox in individuals on ART ($\sigma^T = 1.0$), while in the second panel of same figure, we consider a scenario where HIV infection slightly increases the susceptibility to mpox for these individuals ($\sigma^T = 1.3$). As expected, when HIV increases susceptibility to mpox, the invasion reproduction number increases, which implies more cases of mpox. We also observe from the results in this figure that an increase in Ω decreases $\mathcal{R}_c^{mh}$ for all values of σ for all the scenarios considered here. This implies that the

spread of mpox will be reduced when there are more people on ART at the beginning of an mpox outbreak. More importantly, the burden of mpox decreases as the condom preventability level increases or when the sexual contact rate is reduced in the population. This can easily be seen in the top panel of Fig. 4, where we vary the condom preventability level and the sexual contact rate.

In Fig. 4(a), we observe that when the sexual contact rate is high ($c = 0.85$) and the condom preventability level is low ($\xi = 0.0$), no combination of Ω and σ can bring the mpox invasion reproduction number below 1. Since we already have individuals on ART incorporated into the model and we varied the proportion of individuals on ART at the beginning of the mpox outbreak (Ω), this result suggests that ART alone is not sufficient to control the spread of mpox in the population. As we increased the condom preventability level (Fig. 4(b)) and reduced the sexual contact rate (Fig. 4(c)), we notice a decrease in the invasion reproduction number below 1 for some combination of Ω and σ. This suggest that in addition to ART treatment, an mpox epidemic can be controlled in the population, with either an increase in condom preventability (ξ) or a reduction in sexual contact, or a combination of both.

Next, we study the effect of a reduction in HIV infectiousness due to ART on the invasion reproduction number (Fig. 5). Recall that $0 \leq \eta \leq 1$ describes this reduction in infectiousness in our model, where $\eta = 0$ implies that individuals on ART are not infectious and cannot transmit HIV and $\eta = 1$ means ART does not reduce infectiousness at all. Similar to the results in Fig. 4, we consider two main scenarios based on whether HIV infection increase susceptibility to mpox for those on ART or not. Unlike the case of Fig. 4 where the results are relatively consistent between these two scenarios, the results are qualitatively different in this case for these scenarios. From the top panel of Fig. 5, we observe that the reduction of HIV infectiousness due ART has little effect on the invasion reproduction number when HIV infection does not increase susceptibility to mpox in those on ART ($\sigma^T = 1.0$). This result is relatively consistent as we vary the condom preventability level and the sexual contact rate. As we increase ξ (Fig. 5(b)) and decrease c (Fig. 5(c)), for each values of Ω, the change in the invasion reproduction number as η increases is more than the change observed for the baseline scenario (Fig. 5(a)) with a lower ξ and a higher contact rate (c). Overall, for all values of η considered, $\mathcal{R}_c^{mh}$ decreases as the condom preventability level increases and the sexual contact rate decreases.

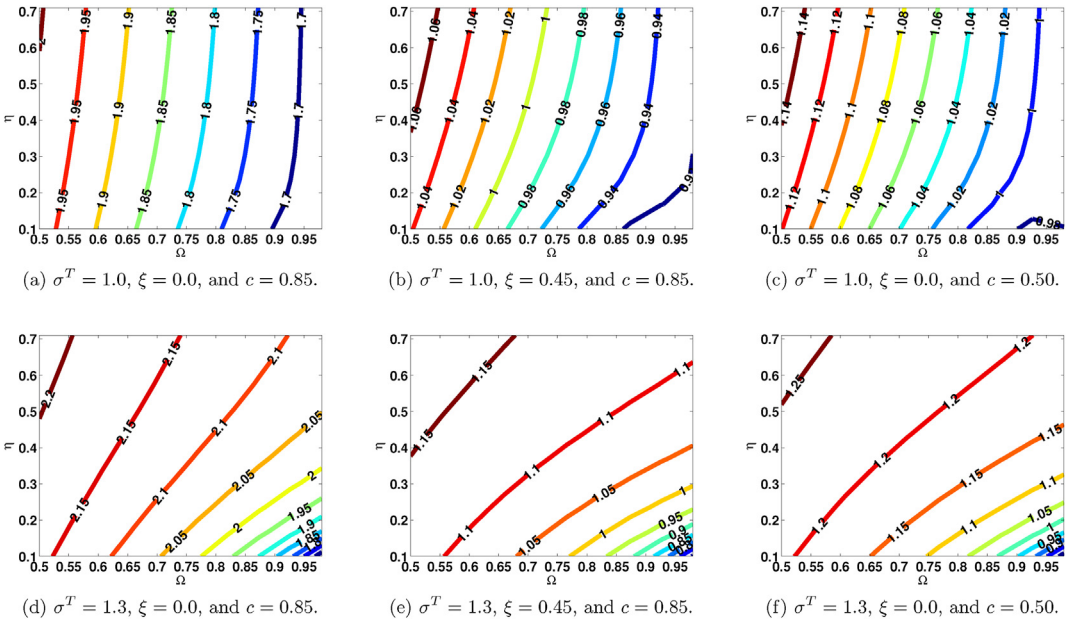
In the lower panel of Fig. 5, where we assume that HIV infection increases susceptibility to mpox ($\sigma^T = 1.3$), reduction in HIV infectiousness due to ART has more effect on the invasion reproduction number compared to the case where $\sigma^T = 1.0$. In other words, an increase in η leads to a higher change in the invasion reproduction number for this scenario than for the scenario with $\sigma^T = 1.0$. This feature is consistent among the three cases we considered that are based on the condom preventability level and sexual contact rate. We also note that the sensitivity of $\mathcal{R}_c^{mh}$ to η is higher when η is smaller and Ω is larger. This corresponds to a scenario where ART is highly effective in reducing HIV infectiousness, and a large fraction of HIV-infected individuals are on ART at the beginning of an mpox outbreak. Comparing the baseline scenarios (Fig. 5(a) and (d)) to



(a) $\sigma^T = 1.0$, $\xi = 0.0$, and $c = 0.85$. (b) $\sigma^T = 1.0$, $\xi = 0.45$, and $c = 0.85$. (c) $\sigma^T = 1.0$, $\xi = 0.0$, and $c = 0.50$.

(d) $\sigma^T = 1.3$, $\xi = 0.0$, and $c = 0.85$. (e) $\sigma^T = 1.3$, $\xi = 0.45$, and $c = 0.85$. (f) $\sigma^T = 1.3$, $\xi = 0.0$, and $c = 0.50$.

Fig. 4. Effect of increased susceptibility to mpox due to HIV infection on mpox invasion reproduction number. Contour plots of mpox invasion reproduction number ($\mathcal{R}_c^{mh}$) in terms of the proportion of HIV-infected individuals on ART at the beginning of mpox outbreak (Ω), the scaling parameter for increased susceptibility to mpox for HIV-infected individuals (σ), and the scaling parameter for increased susceptibility to mpox for HIV-infected individuals on ART (σ^T). Top panel: No increased susceptibility to mpox due to HIV infection ($\sigma^T = 1.0$) and bottom panel: HIV infection increased susceptibility to mpox ($\sigma^T = 1.3$). Parameters used are $\mu = 0.003$, $p_m = 0.15$, $p_h = 0.03$, and $\eta = 0.15$. Remaining parameters are given in the sub-captions and Table 2.



(a) $\sigma^T = 1.0$, $\xi = 0.0$, and $c = 0.85$. (b) $\sigma^T = 1.0$, $\xi = 0.45$, and $c = 0.85$. (c) $\sigma^T = 1.0$, $\xi = 0.0$, and $c = 0.50$.

(d) $\sigma^T = 1.3$, $\xi = 0.0$, and $c = 0.85$. (e) $\sigma^T = 1.3$, $\xi = 0.45$, and $c = 0.85$. (f) $\sigma^T = 1.3$, $\xi = 0.0$, and $c = 0.50$.

Fig. 5. Effect of HIV infectiousness on mpox invasion reproduction number. Contour plots of mpox invasion reproduction number ($\mathcal{R}_c^{mh}$) in terms of the proportion of HIV-infected individuals on ART at the beginning of mpox outbreak (Ω), the scaling parameter for increased susceptibility to mpox for HIV-infected individuals on ART (σ^T), and the scaling parameter for reduction in HIV infectiousness due to ART (η). Top panel: No increased susceptibility to mpox due to HIV infection ($\sigma^T = 1.0$) and bottom panel: HIV infection increased susceptibility to mpox ($\sigma^T = 1.3$). Parameters used are $\sigma = 1.5$, $\mu = 0.003$, $p_m = 0.15$, and $p_h = 0.03$. Remaining parameters are given in the sub-captions and Table 2.

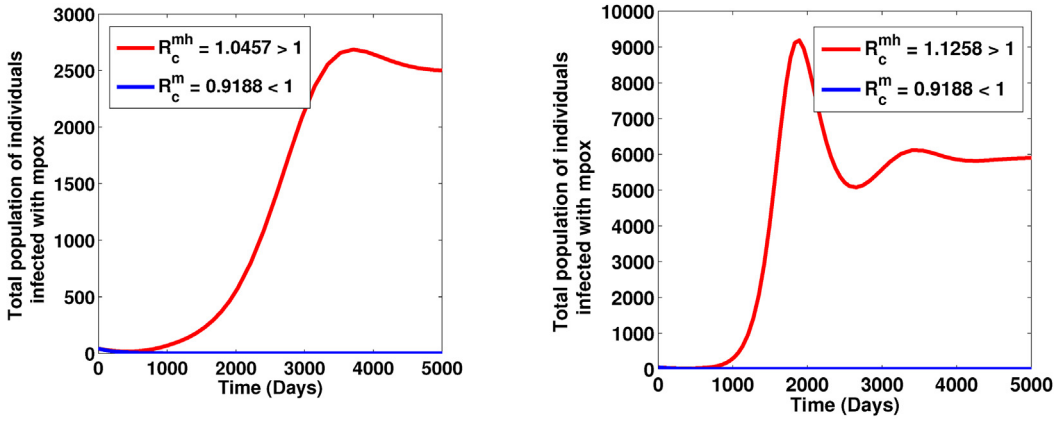
the scenario with increased condom preventability level (Fig. 5(b) and (e)) and that of reduced sexual contact (Fig. 5(c) and (f)), we observe that an increase in ξ decreases the invasion reproduction number more than a reduction in sexual contact rate. Although, the changes in ξ and c are not proportional, these results suggest that the invasion reproduction number may be more sensitive to the sexual contact rate than the condom preventability level.

6. Model simulation

In this section, we simulate the co-infection model (2.1) to investigate the impact of some model parameters on the co-infection dynamics of the two diseases. The simulations are carried out for a period of 5000 days, except in few scenarios when the period was extended to 7000 days (when $\xi = 0.45$ and when $c = 0.50$) to ensure the system stabilizes. We assume that the MSM population in Canada is 4% of its total population at the onset of the 2022–2023 mpox outbreak in the country (May 2022) (Population and total). Based on this, in our simulations, we used $N(0) = N = 4\% \times CN_{pop}$, where $CN_{pop} = 38,929,902$ is the total population of Canada at the beginning of the outbreak (Population and total), as the total MSM population. Other initial conditions are $E_m(0) = 43, I_m(0) = 25, I_h(0) = 15,795, I_h^T(0) = 15,795$. In addition, we assume that there are no individuals in the remaining compartments of our model at the beginning of the outbreak. As a result, we easily compute the initial susceptible population as $S(0) = N(0) - E_m(0) + I_m(0) + I_h(0) + I_h^T(0)$. Note that the initial population for E_m and I_m were chosen based on previous studies to calibrate our model to the 2022–2023 mpox outbreak in Canada (Luigi Bragazzi et al., 2023), while the initial conditions for I_h and I_h^T were chosen based on the prevalence of HIV in the MSM population in Canada (The epidemiology of HIV in).

Fig. 6 shows the dynamics of the total population of individuals infected with mpox in the presence of HIV (red) and absence of HIV (blue). In this figure, we consider two main scenarios: (a) there is no increased susceptibility to mpox for individuals on ART ($\sigma^T = 1.0$), and (b) there is some increased susceptibility to mpox for individuals on ART ($\sigma^T = 1.3$). For both scenarios, mpox cannot spread when there is no HIV in the population (blue). However, with HIV in the population, the mpox invasion reproduction number is greater than 1, which leads to an outbreak of mpox (red). These results show that HIV can facilitate an invasion of mpox into the population and suggest an effective control of HIV may potentially be useful in controlling mpox transmission.

Next, we study the effect of increased susceptibility to mpox due to HIV infection on the size and time for the first peak of the total number individuals infected with mpox ($I_h + I_{hm} + I_{hm}^T$) (Fig. 7). Similar to the results in Fig. 4, when there is moderate reduction in sexual activity ($c = 0.50$), we also consider when there is no increased susceptibility to mpox for those on ART ($\sigma^T = 1.0$) and when there is some increased susceptibility to mpox for those on ART ($\sigma^T = 1.3$). We also examine different scenarios depending on the fraction of HIV-infected individuals on ART at the beginning of an mpox outbreak (Ω) and

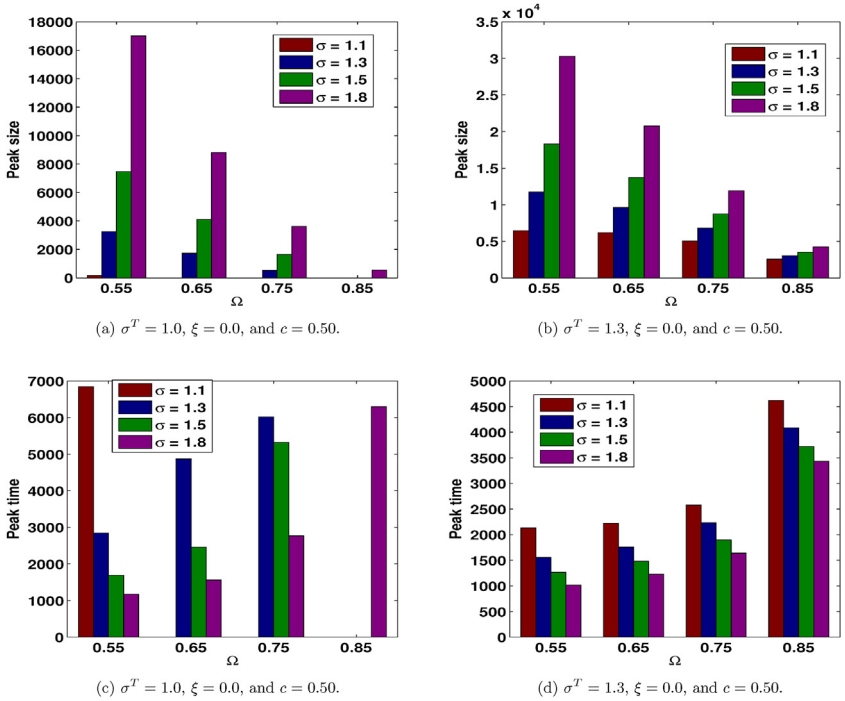


(a) HIV does not increase susceptibility to mpox ($\sigma^T = 1.0$). (b) HIV increases susceptibility to mpox ($\sigma^T = 1.3$).

Fig. 6. Impact of HIV on mpox outbreak. Dynamics of the total population of individuals infected with mpox in the presence of HIV (red) and absence of HIV (blue, computed by setting all the HIV-related parameters to zero in the co-infection model). Left panel: HIV does not increase susceptibility to mpox for the individuals on ART ($\sigma^T = 1.0$) and right panel: HIV increases susceptibility to mpox for the individuals on ART ($\sigma^T = 1.3$). Parameters used are $c = 0.85$, $\xi = 0.45$, $\Omega = 0.5$, $\mu = 0.003$, $p_m = 0.15$, and $\sigma = 1.5$. Remaining parameters are given in Table 2.

variations in the level of enhanced susceptibility to mpox due to HIV infection ($\sigma = 1.1, 1.3, 1.5$, and 1.8). From the top panel of Fig. 7, we observe that there is a significant increase in the peak sizes when HIV infection increases susceptibility to mpox (right panel $\sigma^T = 1.3$) compared to when it does not (left panel $\sigma^T = 1.0$). On the other hand, increase in susceptibility to mpox leads to the first peak happening earlier compared to when HIV does not increase susceptibility (bottom panel of Fig. 7). These results suggest that an mpox outbreak would be larger when ART is not that effective in strengthening immune system and this will lead to the first peak for the total number individuals infected with mpox to happen earlier compared to when ART shows perfect effectiveness. In which case, the peak would be smaller and will happen later.

Similarly, for all values of Ω and σ^T, the peak size increases while the peak time decreases as σ increases. This results show that an increase in susceptibility to mpox among the HIV-infected individuals will also lead to larger mpox outbreaks and the



(a) $\sigma^T = 1.0$, $\xi = 0.0$, and $c = 0.50$. (b) $\sigma^T = 1.3$, $\xi = 0.0$, and $c = 0.50$.

(c) $\sigma^T = 1.0$, $\xi = 0.0$, and $c = 0.50$. (d) $\sigma^T = 1.3$, $\xi = 0.0$, and $c = 0.50$.

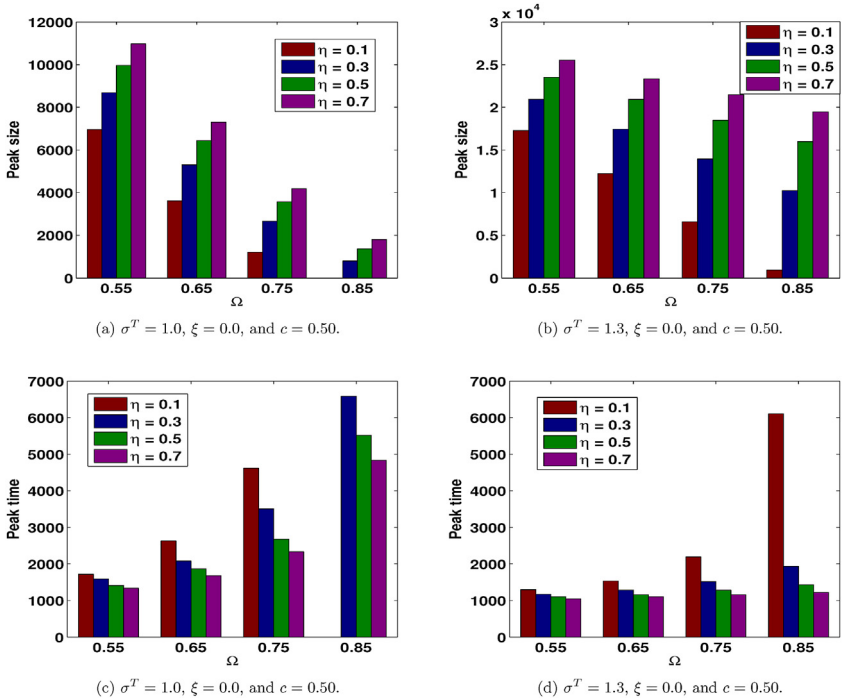
Fig. 7. Effect of increased susceptibility to mpox due to HIV on mpox peak size and time. Barplots of the first peak size (top panel) and the corresponding peak time (bottom panel) for the total number of individuals infected with mpox ($I_h + I_{hm} + I_{hm}^T$), for when HIV does not increase susceptibility to mpox ($\sigma^T = 1.0$, left panel) and when HIV increases mpox susceptibility ($\sigma^T = 1.3$, right panel). A missing bar means there is no outbreak. Parameters used are $\eta = 0.15$, $\mu = 0.003$, $p_m = 0.15$, and $p_h = 0.03$. Remaining parameters are given in the sub-captions and Table 2.

peaks will happen earlier. We notice from the peak sizes in Fig. 7(a) and the corresponding peak times in Fig. 7(c) that for some values of σ, the value of Ω determines whether an outbreak occurs or not. For example, given σ level at 1.1, we only need to achieve 65% treatment coverage to control mpox, while given σ within the range 1.3–1.5, we need to achieve a higher coverage of 85% to eradicate mpox. These results show that for a given level of susceptibility to mpox due to HIV infection, the proportion of HIV-infected individuals on ART can determine whether or not an mpox introduction to an MSM population will be controlled or will lead to an outbreak. Overall, an increase in the proportion of HIV-infected individuals on ART at the beginning of an mpox outbreak (Ω) leads to a decrease in the peak size and an increase in the peak time. This result is important as it emphasizes the importance of having HIV-infected individual on ART as a measure for controlling mpox outbreak in an MSM population. Note that these results agree with the contour plots for $\mathcal{R}_c^{hm}$ in Fig. 4.

In Fig. 8, we study the effect of reduction in HIV infectiousness due to ART (η) on mpox outbreak when there is moderate reduction in sexual activity ($c = 0.50$). Similar to the results in Fig. 5, we determine how reduction in HIV infectiousness due to ART will affect the first peak size and peak time for an mpox outbreak in an MSM population. From Fig. 8(a) and (b), we observe that for each value of Ω, the peak size decreases as HIV infectiousness due to ART decreases. In some instances, e.g., $\Omega = 0.85$, a reduction of HIV infectiousness leads to the invasion reproduction number going below 1 ($\eta = 0.1$), which implies the control of an mpox outbreak. In addition, from Fig. 8(c) and (d), we observe that reduction in HIV infectiousness has limited effect on the peak size when the fraction of HIV-infected individuals on ART at the beginning of an mpox outbreak (Ω) is lower (e.g., $\Omega = 0.55$ and $\Omega = 0.65$) compared to when they are higher (e.g., $\Omega = 0.75$ and $\Omega = 0.85$). Although, HIV infectiousness is not directly related to mpox infections, an increase in HIV infectiousness may lead to an increase in HIV infections, thereby giving rise to mpox cases depending on how much HIV infection influences susceptibility to mpox. These results highlight the potential for controlling mpox spread in an MSM population through HIV treatments that reduces infectiousness. Note that these results also agree with the contour plots for $\mathcal{R}_c^{hm}$ in Fig. 5.

7. Discussion and conclusion

People living with HIV (PWH) have been adversely affected by the 2022–2023 mpox outbreak, accounting for about 40% of diagnosed mpox cases (Mitjà et al., 2023a, 2023b). According to the Centers for Disease Control and Prevention (CDC), PWH are at a higher risk of severe complications from other diseases, including mpox, particularly those with low CD4 counts or who are not virally suppressed. These individuals are more likely to be hospitalized and possibly die if they contract mpox (Centers for Disease Control and Preventione). Here, we used a mechanistic compartmental model to study the dynamics of HIV-mpox co-infection in an MSM population. We investigated the potential effect of HIV spread in the population on the



(a) $\sigma^T = 1.0$, $\xi = 0.0$, and $c = 0.50$. (b) $\sigma^T = 1.3$, $\xi = 0.0$, and $c = 0.50$.

(c) $\sigma^T = 1.0$, $\xi = 0.0$, and $c = 0.50$. (d) $\sigma^T = 1.3$, $\xi = 0.0$, and $c = 0.50$.

Fig. 8. Effect of HIV infectiousness on mpox peak size and time. Barplots of the first peak size (top panel) and the corresponding peak time (bottom panel) for the total number of individuals infected with mpox ($I_h + I_{hm} + I_{hm}^T$), for reduced HIV infectiousness due to ART for when HIV does not increase susceptibility to mpox ($\sigma^T = 1.0$, left panel) and when HIV increases mpox susceptibility ($\sigma^T = 1.3$, right panel). A missing bar means there is no outbreak. Parameters used are $\sigma = 1.5$, $\mu = 0.003$, $p_m = 0.15$, and $p_h = 0.03$. Remaining parameters are given in the sub-captions and Table 2.

dynamics of mpox. This study is motivated by the 2022–2023 mpox outbreak, which disproportionately affected the MSM population (Ortiz-Saavedra et al., 2023). Since HIV is also disproportionately higher in the MSM population (The epidemiology of HIV in; Centers for Disease Control and Prevention, 2020), it is imperative to understand the potential implication of introducing mpox into this population. To the best of our knowledge only a few studies have looked at HIV-mpox co-infection (Bhunu et al., 2012; Ifeanyi Marcus et al., 2024; Odiba Peace et al., 2024; Ogoina et al., 2020), and none of these studies investigated the impact of HIV on mpox spread in an MSM population.

Our co-infection model incorporates the dynamics of both diseases and considers HIV treatment using antiretroviral therapy (ART). Although effective vaccines and treatments are available for mpox (World Health Organization; World Health Organization et al., 2022), we did not incorporate these control measures in our model as we aimed to understand how HIV dynamics can affect mpox spread in the absence of mpox vaccinations and treatment. Our model incorporates a potential increase in susceptibility to mpox due to HIV infection (CDC health advisory) and a decrease in HIV infectiousness due to ART (Cohen et al., 2011; Eisinger et al., 2019; Lima et al., 2021). We also incorporate a sexual contact parameter to modulate the sexual contact rate in the population and investigate its effect on mpox spread. We considered an mpox sub-model (valid in the absence of HIV) and a HIV sub-model (valid in the absence of mpox) in addition to the full co-infection model. We computed the control reproduction numbers for the sub-models and an mpox invasion reproduction number for the co-infection model, which gives the average number of secondary mpox infections generated by a single mpox-infected individual introduced into an HIV-endemic population. The mpox invasion reproduction number is important in our study since HIV is endemic in the MSM population, and we are interested in understanding the dynamics of mpox when HIV is introduced into such a population.

A sensitivity analysis on the mpox control reproduction number using the Latin Hypercube Sampling (LHS) revealed that the reproduction number is positively sensitive to the sexual contact rate and the mpox transmission probability but negatively sensitive to the condom preventability level. An interpretation of this result is that the mpox control reproduction number will increase (more cases per infected individual) when there is more sexual contact and a higher probability of transmission and decrease (fewer cases per infected individual) when the condom preventability level increases. These results are intuitive since an increase in sexual contact and transmission probability will lead to more cases, and more effective use of condoms will decrease transmission. A similar result for the mpox invasion reproduction number shows an increase in sexual contact, transmission probability, HIV infectiousness, and susceptibility to mpox for HIV-infected individuals will increase the invasion reproduction number, leading to more infection per mpox-infected individual at the beginning of an mpox outbreak in a population where HIV is endemic (Fig. 2). On the other hand, an increase in the condom preventability level, the enrollment rate for individuals co-infected with HIV and mpox on ART, and the proportion of HIV-infected individuals on ART at the beginning of an mpox outbreak, will lead to a decrease in the invasion reproduction number. It is important to note that we have little control over many of the parameters listed here. However, we can influence the following: sexual contact rate, condom preventability level, rate of enrollment on ART for those co-infected, and the fraction of HIV-infected individuals on ART at the beginning of an mpox outbreak. Our sensitivity analysis on the invasion control reproduction number suggests that we have a good chance of controlling mpox in an HIV-endemic population by reducing sexual contact and increasing the condom preventability level and the enrollment of individuals living with HIV on ART, either before or during an mpox outbreak.

The results from our scenario analysis (Figs. 4 and 5) further reinforce those from our sensitivity analysis. In these scenario analyses, we explicitly showed the combined effects of the condom preventability level, sexual contact rate, and fraction of HIV-infected individual on ART at the beginning of an mpox outbreak. We showed that, based on the parameter set used in our analyses, HIV treatment with ART may not be sufficient in controlling an mpox outbreak. In other words, we were not able to bring the mpox invasion reproduction number down to below 1 by increasing the fraction of HIV-infected individuals on ART at the beginning of an mpox outbreak, when sexual contact rate is high and condom preventability level is low (Fig. 4(a)). However, by either moderately increasing the condom preventability level (Fig. 4(b)) or reducing the sexual contact rates (Fig. 4(c)), we are able to find fractions of HIV-infected individuals on ART at the beginning of an mpox outbreak, which bring the invasion reproduction number to below 1. These results were verified by simulating the model equation (2.1) and extracting the first peak size and time for the total population of individuals with mpox in the population (Figs. 7 and 8). Some of these results align with those of Bragazzi et al. (Luigi Bragazzi et al., 2023), where they showed that adaptive sexual behavioural change, especially among the high-risk group, could help control the spread of mpox in Canada. Also, Xiridou et al. (Adam et al., 2023), in a mathematical modelling study, showed that, even without mpox vaccination, the level of infection-induced immunity and sexual behaviour change could help curtail the transmission of mpox in the Netherlands.

Another highlight of our study involves showing that the presence of HIV in an MSM population can facilitate the spread of mpox in the population. This analysis was done by showing that, for the same set of parameters, the mpox control reproduction number is less than 1 (mpox cannot spread in the absence of HIV), while the invasion reproduction number is greater 1 (mpox can spread when HIV is endemic in the population) (Fig. 6). This result is important as it emphasizes the impact of HIV endemicity in the MSM population on a potential mpox outbreak in the population. In other words, a potential exposure of the population to an mpox case, that would not have led to the spread of mpox in the population, will lead to an outbreak due to HIV endemicity. This result sets a precedence for protecting the MSM population from an mpox outbreak since HIV is already endemic in the population. Our findings agree with the study by Bhunu et al. (Bhunu et al., 2012), that HIV enhances mpox. In their study, they showed that the presence of HIV in a population caused more mpox cases, as compared to when there is no HIV.

Although many of the parameters used in this study are related to the 2022–2023 mpox outbreak in Canada, our model and its results are applicable to any MSM population with similar characteristics. Some limitations of our model include not considering mpox re-infection, the exposed stage of HIV infection, individuals infected with mpox who became infected with HIV, and mpox vaccination and treatment. Another limitation of this study involves not fitting the model to the mpox and HIV cases data for a specific location. Although this will help calibrate the model to the mpox scenario for that location and improve the model prediction for that location, it is not necessary for our study as we aim to provide a general framework and analysis that can be adapted for any location. Furthermore, our model does not incorporate HIV preventative measures such as the use of pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP). PrEP and PEP are crucial in the fight against HIV. Future study may incorporate the effectiveness of PrEP and PEP not only in preventing HIV but also in potentially reducing susceptibility to mpox infection among high-risk populations like MSM. It would also be important to consider the behavioral, social, and cultural factors that influence the acceptance and use of PrEP and PEP among MSM populations. Factors such as stigma, awareness, and health literacy can significantly affect the effectiveness of these interventions. Lastly, assessing the policy and public health implications of incorporating PrEP and PEP into preventive strategies for HIV and mpox is crucial. This includes evaluating cost-effectiveness, resource allocation, and the potential reduction in healthcare burden. By delving into these areas, future research can offer a more comprehensive understanding of PrEP and PEP's role in preventing HIV and mpox co-infection, especially among MSM populations, contributing to more effective public health strategies.

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CRediT authorship contribution statement

Andrew Omame: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Methodology, Investigation, Formal analysis, Conceptualization. **Qing Han:** Writing – review & editing, Validation, Methodology, Formal analysis, Conceptualization. **Sarafa A. Iyaniwura:** Writing – review & editing, Validation, Investigation, Formal analysis, Conceptualization. **Adeniyi Ebenezer:** Writing – review & editing. **Nicola L. Bragazzi:** Writing – review & editing, Validation, Resources, Conceptualization. **Xiaoying Wang:** Writing – review & editing, Validation. **Jude D. Kong:** Writing – review & editing, Validation, Conceptualization. **Woldegebriel A. Woldegerima:** Writing – review & editing, Visualization, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that there is no competing interest with this publication titled “Understanding the impact of HIV on mpox transmission in an MSM population: a mathematical modeling study”.

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Appendix. A

A.1. Derivation of the control reproduction number for the mpox sub-model

We derive the control reproduction number for the mpox sub-model (3.1) using the next-generation matrix approach (Van den Driessche and Watmough, 2002). The matrix $\mathcal{F}_m$, describing the new infections and matrix $\mathcal{V}_m$ describing all other transitions within the infectious stages of the model are defined as follows

$$\mathcal{F}_m = \begin{pmatrix} \dfrac{c\,p_m(1-\nu\epsilon)I_m}{S+E_m+I_m+R_m}S \\ 0 \end{pmatrix}, \qquad \mathcal{V}_m = \begin{pmatrix} (\alpha+\mu)E_m \\ (\gamma+\delta_m+\mu)I_m - \alpha E_m \end{pmatrix}.$$

Taking the partial derivatives of $\mathcal{F}_m$ and $\mathcal{V}_m$ with respect to the disease classes E_m and I_m and evaluating at the disease free

equilibrium $\Psi_{0m} = \left(\frac{\Lambda}{\mu}, 0, 0, 0\right)$ we have

$$F_m = \begin{pmatrix} 0 & cp_m(1-\nu\epsilon) \\ 0 & 0 \end{pmatrix}, \qquad V_m = \begin{pmatrix} (\alpha+\mu) & 0 \\ -\alpha & (\gamma+\delta_m+\mu) \end{pmatrix}.$$

Thus, the control reproduction number for the mpox sub-model is given by

$$\mathcal{R}_c^m = \rho\left(F_m V_m^{-1}\right) = \frac{cp_m(1-\nu\epsilon)\alpha}{(\alpha+\mu)(\gamma+\delta_m+\mu)}.$$

A.2. Derivation of the control reproduction number of the HIV sub-model

Next, we compute the control reproduction number for the HIV sub-model (3.2) following a similar approach used in Section A.1. In this case, the matrix $\mathcal{F}_h$ and $\mathcal{V}_h$ are defined as follows

$$\mathcal{F}_h = \begin{pmatrix} \frac{cp_h(1-\nu\epsilon)(I_h+\eta I_h^T)}{S+I_h+I_h^T} S \\ 0 \end{pmatrix}, \qquad \mathcal{V}_h = \begin{pmatrix} (\tau+\delta_h+\mu)I_h \\ (\delta_h^T+\mu)I_h^T - \tau I_h \end{pmatrix}.$$

Taking the partial derivatives of $\mathcal{F}_h$ and $\mathcal{V}_h$ with respect to the disease classes I_h and I_h^T and evaluating at the disease free equilibrium $\Psi_{0h} = \left(\frac{\Lambda}{\mu}, 0, 0\right)$ we have

$$F_h = \begin{pmatrix} cp_h(1-\nu\epsilon) & \eta cp_h(1-\nu\epsilon) \\ 0 & 0 \end{pmatrix}, \qquad V_h = \begin{pmatrix} (\tau+\delta_h+\mu) & 0 \\ -\tau & (\delta_h^T+\mu) \end{pmatrix}.$$

Thus, the control reproduction number for the HIV sub-model is given by

$$\mathcal{R}_c^h = \frac{cp_h(1-\nu\epsilon)}{(\tau+\delta_h+\mu)} + \frac{\eta cp_h(1-\nu\epsilon)\tau}{(\tau+\delta_h+\mu)(\delta_h^T+\mu)}.$$

A.3. Derivation of the mpox invasion reproduction number at HIV endemic equilibrium

We now derive the mpox invasion reproduction number around the HIV endemic equilibrium

$$\Psi_{eh} = \left(S^*, 0, 0, 0, I_h^*, I_h^{T*}, 0, 0, 0, 0, 0, 0\right). \tag{A.1}$$

The matrix $\mathcal{F}$, describing the new mpox infections and matrix $\mathcal{V}$ describing all other transitions within the infectious stages of the model are defined as follows

$$\mathcal{F} = \begin{pmatrix} \lambda_m S \\ 0 \\ \lambda_{hm} I_h \\ \lambda_{hm}^T I_h^T \\ 0 \\ 0 \end{pmatrix}, \qquad \mathcal{V} = \begin{pmatrix} (\alpha+\mu)E_m \\ (\gamma+\delta_m+\mu)I_m - \alpha E_m \\ (\tau+\alpha+\delta_h+\mu)E_{hm} \\ (\alpha+\delta_h^T+\mu)E_{hm}^T - \tau E_{hm} \\ (\gamma+\rho\tau+\delta_{hm}+\mu)I_{hm} - \alpha E_{hm} \\ (\gamma+\delta_{hm}^T+\mu)I_{hm}^T - \alpha E_{hm}^T - \rho\tau I_{hm} \end{pmatrix}.$$

Taking the partial derivatives of $\mathcal{F}$ and $\mathcal{V}$ with respect to the disease classes E_m, I_m, E_{hm}, E_{hm}^T, I_{hm} and I_{hm}^T and evaluating at HIV endemic equilibrium A.1 we have

$$F = \begin{pmatrix} 0 & \frac{cp_m(1-\nu\epsilon)S^*}{N^*} & 0 & 0 & \frac{cp_m(1-\nu\epsilon)S^*}{N^*} & \frac{cp_m(1-\nu\epsilon)S^*}{N^*} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \sigma\frac{cp_m(1-\nu\epsilon)I_h^*}{N^*} & 0 & 0 & \sigma\frac{cp_m(1-\nu\epsilon)I_h^*}{N^*} & \sigma\frac{cp_m(1-\nu\epsilon)I_h^*}{N^*} \\ 0 & \sigma^T\frac{cp_m(1-\nu\epsilon)I_h^{T*}}{N^*} & 0 & 0 & \sigma^T\frac{cp_m(1-\nu\epsilon)I_h^{T*}}{N^*} & \sigma^T\frac{cp_m(1-\nu\epsilon)I_h^{T*}}{N^*} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$V = \begin{pmatrix} \alpha+\mu & 0 & 0 & 0 & 0 & 0 \\ -\alpha & \gamma+\delta_m+\mu & 0 & 0 & 0 & 0 \\ 0 & 0 & \tau+\alpha+\delta_h+\mu & 0 & 0 & 0 \\ 0 & 0 & -\tau & \alpha+\delta_h^T+\mu & 0 & 0 \\ 0 & 0 & -\alpha & 0 & \gamma+\rho\tau+\delta_{hm}+\mu & 0 \\ 0 & 0 & 0 & -\alpha & -\rho\tau & \gamma+\delta_{hm}^T+\mu \end{pmatrix}.$$

The mpox invasion reproduction number at HIV endemic equilibrium point is given by the spectral radius of FV^{-1}, which is given by

$$\mathcal{R}_c^{mh} = \mathcal{R}_{c,1}^{mh} + \mathcal{R}_{c,2}^{mh} + \mathcal{R}_{c,3}^{mh}, \tag{A.2}$$

where

$$\begin{aligned} \mathcal{R}_{c,1}^{mh} &= \frac{cp_m(1-\nu\epsilon)\alpha S^*}{(\alpha+\mu)(\gamma+\delta_m+\mu)N^*}, \\ \mathcal{R}_{c,2}^{mh} &= \frac{\sigma c\alpha p_m(1-\nu\epsilon)I_h^*}{(\tau+\alpha+\delta_h+\mu)N^*}\left[\frac{1}{\Phi}+\frac{\rho\tau}{\Phi(\gamma+\delta_{hm}^T+\mu)}+\frac{\tau}{(\alpha+\delta_h^T+\mu)(\gamma+\delta_{hm}^T+\mu)}\right], \\ \mathcal{R}_{c,3}^{mh} &= \frac{\sigma^T cp_m(1-\nu\epsilon)\alpha I_h^{T*}}{(\alpha+\delta_h^T+\mu)(\gamma+\delta_{hm}^T+\mu)N^*}. \end{aligned}$$

Here, $\Phi = \gamma+\rho\tau+\delta_{hm}+\mu$ and N^* is the total population at mpox-free and HIV endemic equilibrium, given by

$$N^* = \frac{\Lambda\left[\left(\delta_h^T+\mu+\tau\right)+(\delta_h^T+\mu)\left(\mathcal{R}_c^h-1\right)+\tau\left(\mathcal{R}_c^h-1\right)\right]}{(\tau+\delta_h+\mu)(\delta_h^T+\mu)\left(\mathcal{R}_c^h-1\right)+\mu(\delta_h^T+\mu+\tau)},$$

where $\mathcal{R}_c^h$ is the HIV associated control reproduction number, which is greater than one at the HIV endemic equilibrium.

In terms of the proportion of HIV-infected individuals on ART at the beginning of an mpox outbreak (Ω), the components of the mpox invasion reproduction number can be written as

$$\begin{aligned} \mathcal{R}_{c,1}^{mh} &= \frac{cp_m(1-\nu\epsilon)\alpha S^*}{(\alpha+\mu)(\gamma+\delta_m+\mu)N^*}, \\ \mathcal{R}_{c,2}^{mh} &= \frac{\sigma c\alpha p_m(1-\nu\epsilon)I_h^*}{\left[\frac{\Omega}{1-\Omega}(\delta_h^T+\mu)+\alpha+\delta_h+\mu\right]N^*}\left[\frac{1}{\Phi}+\frac{\rho\Omega(\delta_h^T+\mu)}{\Phi(1-\Omega)(\gamma+\delta_{hm}^T+\mu)}+\frac{\Omega(\delta_h^T+\mu)}{(1-\Omega)(\alpha+\delta_h^T+\mu)(\gamma+\delta_{hm}^T+\mu)}\right], \\ \mathcal{R}_{c,3}^{mh} &= \frac{\sigma^T cp_m(1-\nu\epsilon)\alpha I_h^{T*}}{(\alpha+\delta_h^T+\mu)(\gamma+\delta_{hm}^T+\mu)N^*}, \end{aligned}$$

where

$$S^* = \frac{\Lambda}{\lambda_{hs}^* + \mu}, \qquad I_h^* = \frac{\lambda_{hs}^* S^*}{\left[\frac{\Omega}{1-\Omega}(\delta_h^T + \mu) + \delta_h + \mu\right]}, \qquad I_h^{T*} = \frac{\Omega}{(1-\Omega)} I_h^*,$$

$$\lambda_{hs}^* = \frac{\left[\frac{\Omega}{1-\Omega}(\delta_h^T + \mu) + \delta_h + \mu\right]\left(\delta_h^T + \mu\right)}{\left[\delta_h^T + \mu + \frac{\Omega}{1-\Omega}(\delta_h^T + \mu)\right]}\left(\mathcal{R}_c^h - 1\right), \qquad N^* = S^* + I_h^* + I_h^{T*},$$

$$\mathcal{R}_c^h = \frac{c\, p_h (1 - \nu\epsilon)}{\left[\frac{\Omega}{1-\Omega}(\delta_h^T + \mu) + \delta_h + \mu\right]} + \frac{\eta c\, p_h (1 - \nu\epsilon)\left[\frac{\Omega}{1-\Omega}(\delta_h^T + \mu)\right]}{\left[\frac{\Omega}{1-\Omega}(\delta_h^T + \mu) + \delta_h + \mu\right]\left(\delta_h^T + \mu\right)}.$$

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