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RESEARCH ARTICLE

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Adaptive changes in sexual behavior in the high-risk population in response to human monkeypox transmission in Canada can help control the outbreak: Insights from a two-group, two-route epidemic model

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Abstract

Monkeypox, a zoonotic disease, is emerging as a potential sexually transmitted infection/disease, with underlying transmission mechanisms still unclear. We devised a risk-structured, compartmental model, incorporating sexual behavior dynamics. We compared different strategies targeting the high-risk population: a scenario of control policies geared toward the use of condoms and/or sexual abstinence (robust control strategy) with risk compensation behavior change, and a scenario of control strategies with behavior change in response to the doubling rate (adaptive control strategy). Monkeypox's basic reproduction number is 1.464, 0.0066, and 1.461 in the high-risk, low-risk, and total populations, respectively, with the high-risk group being the major driver of monkeypox spread. Policies imposing condom use or sexual abstinence need to achieve a 35% minimum compliance rate to stop further transmission, while a combination of both can curb the spread with 10% compliance to abstinence and 25% to condom use. With risk compensation, the only option is to impose sexual abstinence by at least 35%. Adaptive control is more effective than robust control where the daily sexual contact number is reduced proportionally and remains constant thereafter, shortening the time to epidemic peak, lowering its size, facilitating disease attenuation, and playing a key role in controlling the current outbreak.

KEYWORDS

basic reproduction number, Bayesian framework, Canada, doubling rate, mathematical modeling, men having sex with men (MSM), monkeypox, risk compensation, sexual behavior dynamics

1 | INTRODUCTION

Monkeypox is an emerging zoonotic disease, the infectious agent of which is an Orthopoxvirus, namely, the monkeypox virus,[1] which shares genomic and morphological features with another Orthopoxvirus, the Variola virus (VARV),[2] a deadly pathogen responsible for smallpox. While the latter infectious disease was eradicated in 1980,[3] the former is still circulating, being endemic in a number of African countries, since 1970,[4] and sporadically detected outside of Africa, including the United Kingdom, the United States of America, Singapore, and Israel.

Starting from the end of April 2022, a monkeypox outbreak is ongoing. The epidemiological and clinical features of this outbreak differ from those observed for the previous ones.[5] Sexual transmission has been hypothesized as the major transmission route for the current outbreak, with the community of men having sex with men (MSM) disproportionately and dramatically affected.[4] According to a large-scale, multicountry study, out of 528 monkeypox infections, the transmission was hypothesized to have occurred more likely via sexual intercourse in 95% of the cases.[6] The monkeypox virus has also been isolated from semen samples collected during the early phase of infection in patients with seminal viral shedding.[7] However, other transmission routes have been described as well, including contact with infected animals,[8] travel to endemic countries,[9] occupational exposures,[10] and social and household contact.[11] As such, monkeypox should not be considered an exclusively sexually transmitted disease/infection (STD/STI) but a communicable disease, the transmission of which has been hypothesized to be associated with sexual contact[12] or exposure to sexual networks. This is an important distinction because we are still unsure about the precise transmission mechanisms, that is to say whether contagion is occurring through body fluids exchanged during sexual intercourse, or via contact with mucosal surfaces, scarification, or even respiratory exposures via droplets.[13] On the other hand, this new epidemiological trend seems to suggest that the monkeypox virus may have mutated,[14] adapted, and found a niche in high income countries among subjects with patterns of high frequencies of close, physical contact, like the MSM community.[15]

Canada has become one of the most affected countries in the WHO Region of the Americas, reporting 1400 monkeypox cases (2.1% of all the cases worldwide), across 9 provinces or territories, 38 of which requiring hospitalization. No fatalities have been reported.[16] The first cases of monkeypox virus infections in Canada (2 infected individuals) were reported in Montreal, Quebec province, on May 19, 2022.[17]

Mathematical modeling plays a key role in monitoring, controlling and forecasting infectious disease outbreaks,[18] helping and assisting public health decision- and policy-makers in the design and implementation of specific measures. Mathematical models have also been devised to study, track, predict the dynamics of STDs/STIs, and assess the effectiveness of packages of public health interventions.[19] In the last years, some mathematical models have been developed to study the transmission dynamics of monkeypox[5,13,20–26]: many of these studies presented endemic models of the disease and were published before the current outbreak of monkeypox, or, if devised during the current epidemic, they do not realistically incorporate sexual behaviors of the MSM community, and do not divide the human population into high-risk and low-risk groups and subdivide each group into SEIQR compartments.

Therefore, the present study was undertaken to fill this gap in knowledge.

2 | METHODS

2.1 | Mathematical model

We develop a deterministic, compartmental SEIQR model to study the transmission dynamics of monkeypox. Our model stratifies the population into two groups: *high-risk* and *low-risk* groups. Each group is divided into five compartments: susceptible (S), exposed (E), infectious (I), quarantined (Q), and recovered/removed (R). A susceptible individual becomes infected at some rate upon coming into contact with an infectious individual. We categorize contacts into two forms: sexual and nonsexual (social). Sexual contacts are considered in the high-risk group only since the majority of monkeypox cases in this group are believed to occur through sexual contact, and transmission through sexual contact in the low-risk group is negligible.[11] Furthermore, we considered nonsexual contact.

Since our study is over a short period, we do not consider the transition of individuals from the high-risk group to the low-risk group, and vice versa, and we do not consider natural birth or death demographic rates. Individuals in these two groups interact with each other and can cause disease transmission across the groups. In other words, an infected individual in either of the two groups can infect susceptible individuals in both groups (see the red dashed lines in (Figure 1). These interactions are captured in the force of infection

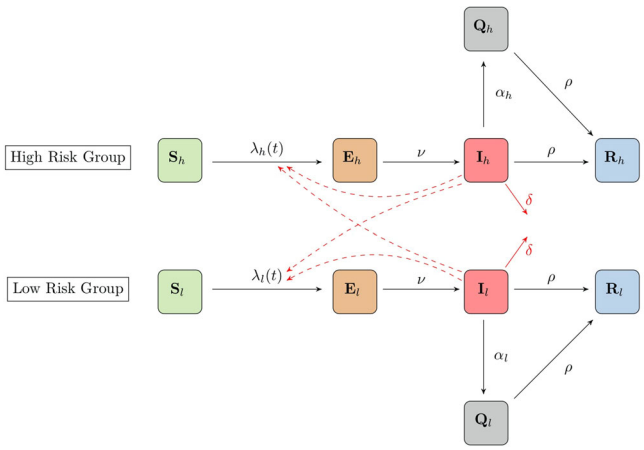

FIGURE 1 Model schematic diagram. Compartments are: susceptible (S), exposed (E), infectious (I), quarantined (Q), and recovered/removed (R). The population is stratified into two groups: high-risk (subscript h) and low-risk (subscript l). The black solid arrows show the transition of individuals through the different stages of monkeypox disease at the rates indicated beside the arrows, the red solid arrows indicate deaths due to monkeypox, and red dashed arrows indicate disease transmission (see [2.1] for more details).

(2.2). Infectious individuals quarantine at a constant rate. We assume that quarantine happens on the first day of their infectious period and that quarantined individuals do not infect anyone. They transition to the recovered compartments upon recovering from the disease.

Figure 1 shows the schematic diagram of our model, where the compartments with subscript h and l represent the high- and low-risk groups, respectively. The black solid arrows show the transition of individuals through the different stages of monkeypox disease and the red solid arrows represent deaths due to monkeypox. The red dashed arrows show disease transmission.

The differential equations of the model are given as follows:

$$\begin{aligned} \frac{dS_h}{dt} &= -\lambda_h S_h \quad \frac{dE_h}{dt} = \lambda_h S_h - vE_h \quad \frac{dI_h}{dt} = vE_h - (\alpha_h + \rho + \delta)I_h \\ \frac{dQ_h}{dt} &= \alpha_h I_h - \rho Q_h \quad \frac{dR_h}{dt} = \rho I_h + \rho Q_h \quad \frac{dS_l}{dt} = -\lambda_l S_l \\ \frac{dE_l}{dt} &= \lambda_l S_l - vE_l \quad \frac{dI_l}{dt} = vE_l - (\alpha_l + \rho + \delta)I_l \\ \frac{dQ_l}{dt} &= \alpha_l I_l - \rho Q_l \quad \frac{dR_l}{dt} = \rho I_l + \rho Q_l, \end{aligned} \tag{2.1}$$

where v is the mean rate of transitioning from the exposed to infectious compartment ($1/v$ is the mean incubation period), ρ is the recovery rate ($1/\rho$ is the mean recovery period), δ is the per-capita disease-induced death rate, and α_h (α_l) is the quarantine rate for infectious individuals in the high- (low-) risk group. We assume that disease-induced death happens in the infectious population only. Here, λ_h and λ_l are the forces of infection for the high- and low-risk groups, respectively, defined as

$$\begin{aligned} \lambda_h &= \frac{\beta^s C^s I_h}{N_h - Q_h} + \frac{\beta C_{hh} I_h}{N_h - Q_h} + \frac{\beta C_{hl} I_l}{N_l - Q_l}; \\ \lambda_l &= \frac{\beta C_{ll} I_l}{N_l - Q_l} + \frac{\beta C_{lh} I_h}{N_h - Q_h}, \end{aligned} \tag{2.2}$$

where β^s and β are the transmission probabilities of monkeypox per sexual and nonsexual contact, respectively, C^s is the average per-capita sexual contact per day (for high-risk group), C_{hh} (C_{ll}) is the average per-capita nonsexual contact per day within the high- (low-) risk group, and $C_{lh} = C_{hl}$ is the average per-capita nonsexual contact per day between individuals in the high- and low-risk groups. Here, N_h and N_l are the population sizes for the high- and low-risk groups, respectively, and $N = N_h + N_l$ is the total human population size. In the equation of the force of infection for the high-risk group (λ_h), the first term accounts for infections in the high-risk group that are due to sexual contact among individuals in the high-risk group, the second term refers to the infections that are due to nonsexual interactions within the high-risk group, and the third term accounts for infections that are due to nonsexual interactions between the low- and high-risk groups. Similarly, the first term in the force of infection for the low-risk group (λ_l) represents infections in the low-risk group that are due to nonsexual contact within the low-risk group, while the second term accounts for infections in the low-risk group that are due to nonsexual contact between the low- and high-risk groups. We have omitted disease transmission due to sexual contact in the low-risk group because monkeypox transmission through this route is minimal in the low-risk group.[6] We have also omitted infections that are due to intergroup sexual contact for the same reason.

2.2 | Sexual behavior change

2.2.1 | Behavior change in response to cumulative monkeypox cases

We consider the possibility where individuals in the high-risk group adjust their sexual behavior as the cumulative cases (T_C) increase, and define the average per-capita sexual contacts per day C^s as

$$C^s = C^s_{\max} - \eta(C^s_{\max} - C^s_{\min}), \tag{2.3}$$

where $C^s_{\max}$ and $C^s_{\min}$ are the maximum and minimum possible per-capita sexual contacts per day for the high-risk group. The parameter η ($0<\eta<1$) models the reduction in sexual contacts and is given by

$$\eta = \frac{[C_T - C_{C_T}]_+}{[C_T - C_{C_T}]_+ + C_0 - C_{C_T}}, \tag{2.4}$$

where $[z]_+ = \max(z, 0)$. Here, C_0 is cumulative case doubling rate that leads to half of the maximal behavioral change, and C_{CT} is the critical threshold disease doubling rate to induce behavioral change. Let the number of cumulative cases be denoted by $T_C(t)$, where

$$T'_C(t) = v[E_h(t) + E_l(t)], \tag{2.5}$$

then C_T in (2.4) being the doubling rate of cumulative cases is calculated as

$$C_T(t) = \frac{T'_C(t)}{T_C \ln 2}. \tag{2.6}$$

2.2.2 | Risk compensation behavior change

Besides, we consider the possibility of risk compensation behavioral change among the high-risk group. As long as the perceived risk of infection is kept at the same level, a consistent practice of protective behavioral strategies for example, condom using, may lead to more sexual encounters as a compensation. If we define the initial risk as

$$\text{Risk} = 1 - \left[1 - \beta^s \frac{I_h(0)}{N_h}\right]^{C^s} \tag{2.7}$$

and assume that high-risk individuals tend to maintain their risk level, then (2.7) leads to the following relationship between C^s and β_s:

$$\frac{C^s}{C^s_{\text{baseline}}} = \frac{ln\left[1 - \beta^s_{\text{baseline}} \frac{I_h(0)}{N_h}\right]}{ln\left[1 - \beta^s \frac{I_h(0)}{N_h}\right]} \tag{2.8}$$

where $\beta^s_{\text{baseline}}$ and C^s_{baseline} are values from Table 1 or otherwise specified. This formulation is derived based on the same idea as in.[32]

TABLE 1 Model parameters, description, and values.

Parameter	Description	Value	95% HDI	Reference
1/v	Mean incubation period	8.5 days		27, 28
1/ρ	Mean infectious period	21 days		27
δ	Per-capita disease-induced death rate	0		16
β^s	Transmission probability per sexual contact	0.24	[0.2–0.3]	Fitted
ε	Scaling factor of transmission probability via nonsexual contact to transmission probability via sexual contact	0.00025	[0.00018–0.00032]	Fitted
β	Transmission probability per nonsexual contact	$\varepsilon\beta^s$		Assumed
C^s	Average per-capita sexual contacts per day	1.2 day^{-1}	[0.92–1.6]	Fitted
C^s_{max}	Maximum average per-capita sexual contacts per day	1.2 day^{-1}		Assumed
C^s_{min}	Minimum average per-capita sexual contacts per day	1/365 day^{-1}		Assumed
C_{ll}	Average per-capita nonsexual contacts per day within low-risk population	10.8 day^{-1}		29
$C_{lh} = C_{hl}$	Average per-capita nonsexual contacts per day between low-risk and high-risk population	10.8 day^{-1}		29
C_{hh}	Average per-capita nonsexual contacts per day within high-risk population	10.8 day^{-1}		29
$\alpha_h = \alpha_l$	Quarantine rate for infectious high-/low-risk individuals	0.15 day^{-1}	[0.13–0.18]	Fitted
N	Total population of Canada	38 000 000		30
N_h	High-risk population size	4% × N		31
N_l	Low-risk population size	96% × N		30
$I_h(0)$	Initial infected high-risk population	25	[21–29]	Fitted
$I_l(0)$	Initial infected low-risk population	2.5	[0.098–4.9]	Fitted

Abbrevitation: HDI, high density interval.

Model parameters, their descriptions and values are summarized in Table 1. Concerning the MSM population size, there is currently no consensus on how to estimate it in a reliable and unbiased fashion. Based on a systematic literature review,[31] we computed the average value of the estimates reported in the literature. We used this percentage to calculate the population of the high-risk group in our model. Estimated parameters are provided with 95% high density interval (HDI). We assume that there are no disease-induced death rates ($\delta = 0$) when fitting our model to data since no monkeypox deaths have been reported in Canada.[16]

2.3 | Data

We collected the daily reported cases (7-day rolling average of confirmed cases) of monkeypox for Canada from May 19, 2022 to July 25, 2022 from Our World in Data.[33] We assume that there were no control measures in place during this period. As of July 23, 2022, the Government of Canada had, indeed, just started the rolling-out of monkeypox vaccination, by deploying over 70 000 doses of vaccines to provinces and territories as public health response to the ongoing monkeypox outbreak.

The data from Our World in Data is not disaggregated into the high-risk and low-risk populations. To disaggregate the data, we assume that all of the people in the high-risk group in Canada are from the MSM community. Thus, since 95% of the reported cases so far are from the MSM community,[30] we extracted 95% of the reported data and attribute it to the high-risk population and 5% to the low-risk population. We equally used the fact that 4% of the 38 million Canadians belong to MSM community,[30] to estimate the total population in each group. From the model equations, $vE_h(t)$ and $vE_l(t)$ are used directly as the simulated 7-day rolling average of confirmed cases from the high- and low-risk groups.

2.4 | Parameter estimation and uncertainty

We only estimated the parameters whose ranges have not been reported in literature. These include the transmission rate of monkeypox through sexual contact, nonsexual contact, quarantine rate, and the initial infected population in each group. The values and sources of the other model parameters are reported in Table 1. Parameter estimation and uncertainty propagation were performed using a Bayesian inference framework that uses Hamiltonian Monte

TABLE 2 Parameter ranges and distributions for sensitivity analysis.

Parameter	Lower bound	Upper bound	Distribution
β^s	0	β^{s*}	U
β	0	β^*	U
C^s	C^{s*}_{min}	2	T
C_{hh} ($=C_{ll} = C_{hl} = C_{lh}$)	1	C^*_{hh}	U
α_h ($=\alpha_l$)	1/8	1	T

Note: T indicates triangular distribution with its peak value from Table 1. U indicates uniform distribution. * indicates values from Table 1.

Carlo to obtain samples from the posterior distribution. We used 500 samples and 500 tuning samples. We used uniform distribution (uninformed) for the prior distributions of the parameters. The prior distributions used in our Bayesian inference for the various parameters are as follows

$$\beta^s \sim U[0,1], \varepsilon \sim U[0,1], \alpha_h \sim U[0,1], C^s \sim U[0,5],$$
$$I_h(0) \sim U[0,95], I_l(0) \sim U[0,5]$$

We employ the following R^2 as the evaluation measure $R^2 = 1 - \frac{\sum_{i=1}^{n}(y_i - y_i)^2}{\sum_{i=1}^{n}(y_i - \bar{y}_i)^2}$, where $\bar{y_i}$ and $\hat{y_i}$ are the mean of the observed and predicted cases, respectively.

2.5 | Sensitivity analysis

We performed sensitivity analysis to investigate the impact of policy-related parameters on the control reproduction number (R_c) and the epidemic peak time and size. For each parameter, Latin hypercube sampling[34,35] is adopted to generate values with distributions and ranges as specified in Table 2. For this analysis, we generated 3000 sets of parameter values. Based on the generated parameter sets, partial rank correlation coefficients (PRCC) were calculated[36] to determine the influence of varying each parameter on R_c and the epidemic peak time and size. The PRCC indices range between −1 and 1, with positive (negative) values indicating a positive (negative) relationship, and magnitudes indicating level of impact: a magnitude of 0 has almost no impact whereas a magnitude of 1 has the most influential impact.

2.6 | Non pharmaceutical interventions with and without risk compensation

We use numerical simulations to study the impact of different control measures on the sexual behavior of the high-risk population and the dynamics of monkeypox in the population. In particular, we look at adaptive changes in sexual behavior related to decrease in frequency of sexual activities and/or related to consistent use of condoms as a result of awareness campaigns and public health policies. We equally look at a scenario in which people in the high-risk group adjust their sexual behaviors based on the doubling rate of cases, and explore how that can impact the spread of monkeypox in the population.

We simulated as well a scenario in which some behavioral adaptations may be attempts to maintain a certain level of sexual health risk deemed as acceptable,[32] compensating either against situations that can pose a risk increase and/or interventions aimed at reducing that risk and forsaking safer sexual practices[37] —this is known as the "sexual health risk compensation strategy."[38] Another slightly different strategy is based on the "sexual health risk homeostasis," in which the acceptable risk level is kept constant (adapted from the "risk homeostasis theory"),[39,40] even though, given the complexity and heterogeneity of sexual behaviors, this theoretical framework positing a "complete" sexual health risk compensation may sound less realistic. The sexual risk compensation strategy in a real-life scenario can be defined as an increase in risk-related behaviors when STD-related risk perception at the individual or community/population level is perceived as lessened or is actually reduced, for example by a biomedical/preventative intervention,[41] as "the rewards of risk-taking become more attractive and engender a compensatory increase in risk-taking."[42]

Changes in sexual behavior can target specific STDs or STDs in general and include: (i) condom-related protective behavioral strategies (PBSs), such as consistent use of condoms, (ii) enhanced STD testing and seeking medical care for STDs, including self-testing and self-diagnosis, (iii) taking prophylactic measures (like preexposure, PrEP, or postexposure, PrEP),[43] (iv) vaccinating against vaccine-preventable STDs, (v) intentional choice of sex partners (either commercial or noncommercial individuals on anti-retroviral therapy, leveraging the "treatment as prevention" (TasP) strategy, which enables achieving an undetectable HIV viral load and effectively prevents passing the virus,[44] (vi) decreasing the number of sex partners, and (vii) decreasing the frequency of sexual acts. We did not explore all sexual behaviors, limiting our model and scenario analysis to condom-related PBSs and frequency of sexual activities.

3 | RESULTS

3.1 | Parameter estimation and uncertainty

The mean of estimated parameters along with the 95% HDI are summarized in Table 1. Figure 2 contains the mean of the posterior predictive samples with their 95% confidence interval. We obtained an R^2 value of 0.81 which indicates a good fit.

3.2 | The basic reproduction numbers

Using the parameter values in Table 1, we estimated that the basic reproduction number in the high-risk population is $R_{h0} = 1.464$, in the low-risk population is $R_{l0} = 0.0066$ and in the total population is

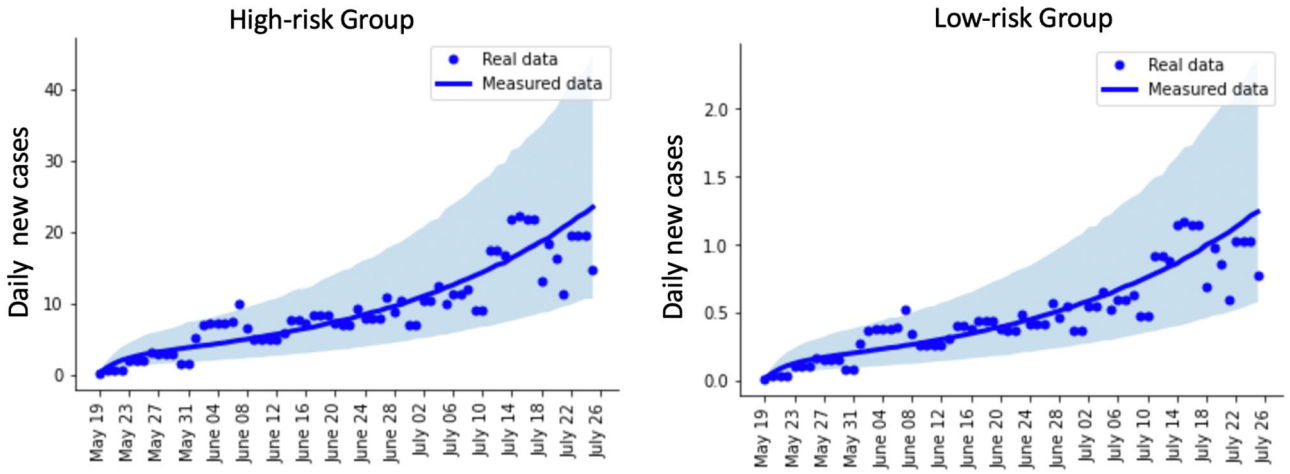

FIGURE 2 Mean model prediction and measured cases. High-risk group (left) and low-risk group (right). Blue dots are the daily new cases (7-day rolling average of confirmed cases), solid blue lines are the mean of the posterior predictive samples, and the colored areas show 95% high density intervals (HDI) of prediction.

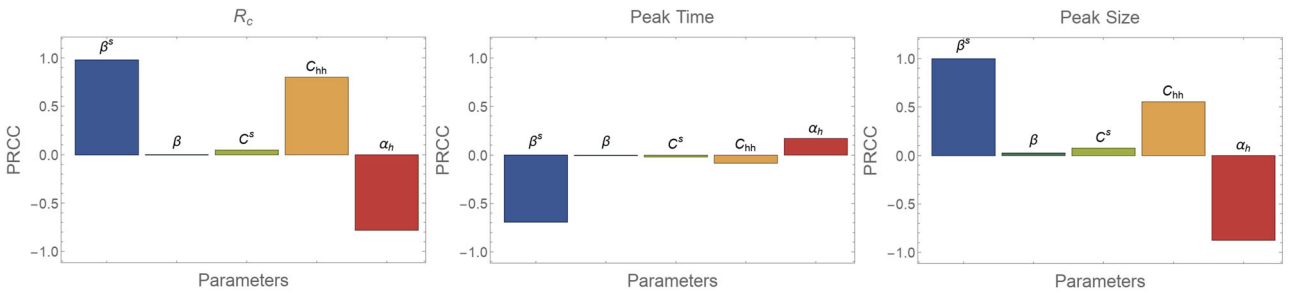

FIGURE 3 Computed partial rank correlation coefficients (PRCC). Calculated PRCC using parameter values from Latin hypercube sampling with respect to the control reproduction number, Rc (left), days to reach epidemic peak (middle), and magnitude of the epidemic peak of monkeypox (right).

$R_0 = 1.461$, implying that members of the high-risk group are the major drivers of monkeypox spread in Canada. For the calculation of the basic reproduction numbers, see Supporting Information material.

3.3 | Sensitivity analysis

Figure 3 shows the PRCC indices of selected parameters on the control reproduction number (R_c). The quarantine rate $\alpha_h(\alpha_l)$ has a negative impact on R_c, while the sexual and nonsexual contact rates, and the disease transmission probabilities have positive impacts. Of the two transmission probabilities in our model, the sexual transmission probability (β^s) outweighs the nonsexual transmission probability (β). This suggests a much higher risk of monkeypox transmission through sexual contact routes within the high-risk population. Among the sexual and nonsexual contact rates, C_{hh} ($=C_{hl} = C_{lh} = C_{ll}$) is more influential, which may be due to the overwhelmingly larger population size of the entire population, suggesting that once transmitted to the general population, monkeypox may thereafter quickly invade. The control reproduction number is also significantly sensitive to the quarantine rate in the sense that practicing more quarantine results in the reduction of monkeypox cases. Figure 3 shows the effects of the PRCC indices on the peak time. The impacts of these parameters are reversed whereas their relative levels of influential power still exhibit a similar pattern. Lastly, Figure 3 shows the effects of the PRCC indices on the epidemic peak size. The magnitudes of impacts of these parameters resemble those observed in Figure 3.

3.4 | Control strategies without adaptive behavior change in high-risk population

In this section, we performed scenario analysis for tentative control strategies in the case of no spontaneous adaptive sexual behavioral change within the high-risk group. Figure 4 shows contour plots of the control reproduction number (R_c) with respect to different pairs of control parameters. In Figure 4, we plot R_c against the sexual and nonsexual transmission probabilities, β^s and β, respectively. Apparent from the figure, reducing β hardly affects R_c, but a 35% reduction in

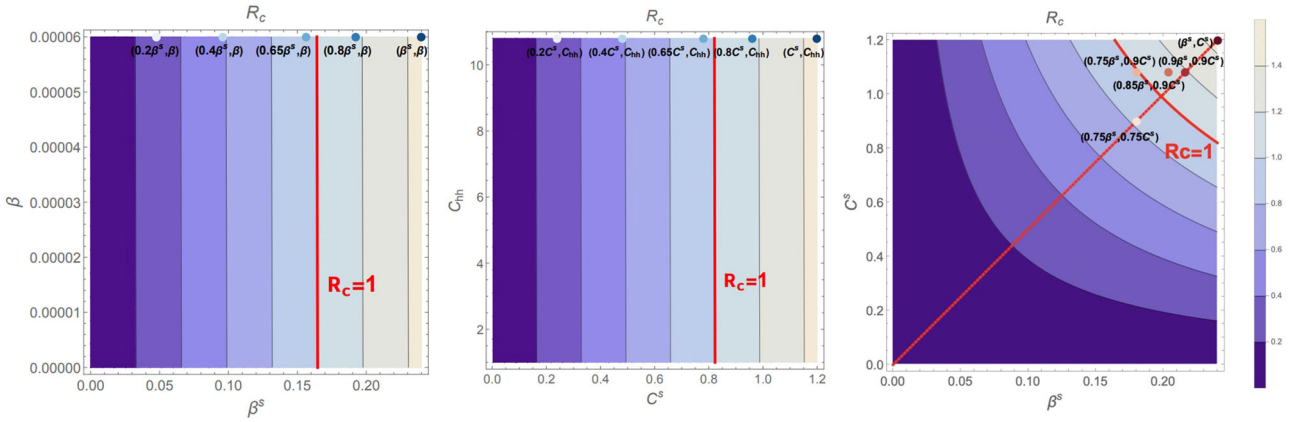

FIGURE 4 Contour plots of the control reproduction number (Rc). Control reproduction number plotted with respect to different pairs of control parameters of the model. The red curve indicates the contour where $R_c = 1$. Dots of corresponding colors represent selected pairs of control parameters used in scenario projections presented in Figure 5.

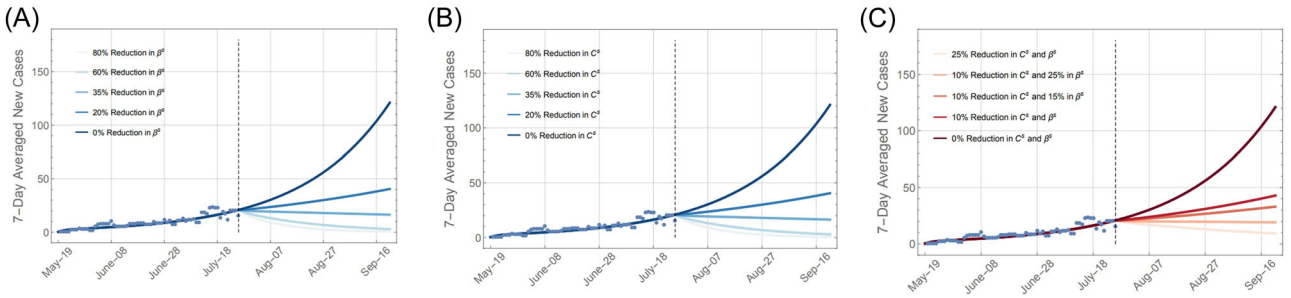

FIGURE 5 Predictions of 7-day averaged daily new cases with various controls. (A) Only imposing condom use (varying βs). (B) Only imposing sexual abstinence (varying Cs). (C) Combination of condom use and abstinence (varying βs and Cs).

β^s is sufficient to bring the reproduction number below 1, keeping the other parameter values fixed. Similarly, in Figure 4, controlling nonsexual contact rates in the population is rather inefficient compared to containing sexual contact rates in the high-risk population. These results imply that a policy geared toward either use of condoms or sexual abstinence in the high-risk population can more effectively and sufficiently mitigate the current monkeypox outbreak in Canada than a policy geared toward the reduction of nonsexual contacts in the general population. Furthermore, Figure 4 suggests that the rate of sexual contacts and the sexual transmission probability have exact same effects on the control of the spread of the disease (the red solid line represents equal amounts of reduction of the two parameters and it is equally bisecting the entire contour plot). This is also obvious from the formulation of sexual force in infection as it is the simple product of C^s and β^s. Several combinations of parameter pairs are selected from the this figure to generate scenario-based projections in Figure 5.

In these projections, policy of imposing only condom use (Figure 5A) or policy of imposing only sexual abstinence (Figure 5B) need to achieve a minimum compliance rate of more than 35% to successfully stop further transmission of monkeypox. But a combination of both can more easily curb the disease spread if there is 10% compliance to abstinence and 25% to condom use. This suggests a combination of control measures within the high-risk group is the most efficient way to contain the current outbreak of monkeypox in Canada.

With risk-compensation behavior change in the high-risk population in place as formulated in (2.8), the effectiveness of these robust controls will be weakened. A simple reduction in transmission probability can hardly curtail the reproduction number, and therefore sexual abstinence is absolutely needed in this situation. In this case, a 35% reduction in sexual contact rate is the minimum required. Details are given in Supporting Information material.

3.5 | Control strategies with adaptive behavior change in response to the doubling rate in high-risk population

We explore in addition how adaptive behavior change may mitigate the spread of monkeypox. The daily sexual contact number for the high-risk group reduces according to the formulation in (2.4). Figure 6A shows that the daily sexual contact number reduces gradually over time. Here we fix all the parameters as shown in

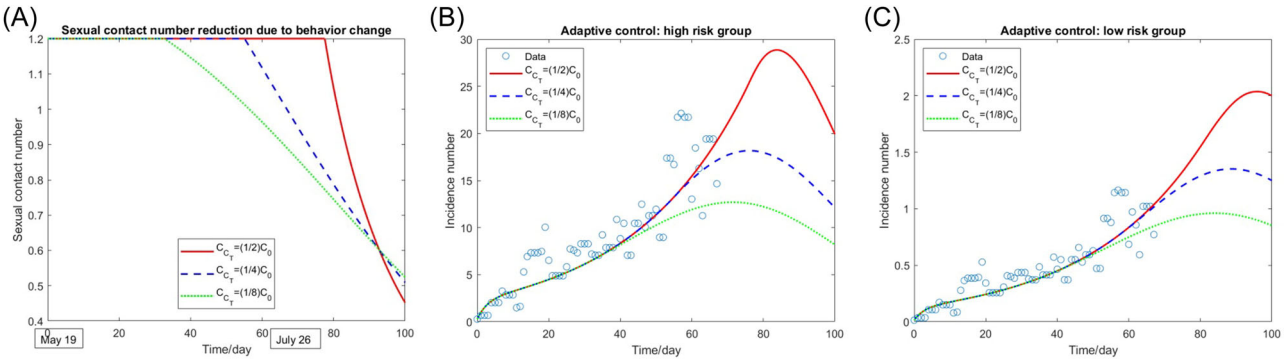

FIGURE 6 Effect of adaptive behavior change on disease dynamics. (A) Adaptive change of sexual contact rates among the high-risk group. (B–C) Daily incidence number for the high and low risk groups, respectively, when behaviors change adaptively.

Table 1 expect for C_0 and C_{CT}. We choose the half-saturation constant C_0 as 80% of the maximum of the cumulative case doubling rate, that is, $C_0 = (4/5)$ max C_T and vary the critical case doubling rate C_{CT} to be $(1/2)C_0$, $(1/4)C_0$, and $(1/8)C_0$, respectively. The smaller the critical case doubling rate is, the earlier individuals in the high-risk group proactively reduce their daily sexual contact numbers as protective measures. According to,[28] by the end of approximately 90 days, the daily sexual contact number among the MSM community reduces to 50% of the original level. We test extensively and find out that $C_0 = (4/5)\max C_T$ leads to the best match to the reported cases of monkeypox in Canada.

Figure 6B–C demonstrate the projection for the high-risk and low-risk groups by using the adaptive control strategy. The results in this figure suggest that adaptive control is more effective compared to the robust control where the daily sexual contact number is reduced proportionally and remains as a constant thereafter. The adaptive behavior changes among the high-risk group significantly shorten the time to epidemic peak, lower the epidemic peak size, and facilitate the attenuation of the disease.

4 | DISCUSSION AND LIMITATIONS

Our study shows that the way individuals in the high-risk group change their sexual behavior (in terms of direction and extent) is fundamental to controlling the current monkeypox outbreak in Canada. Sexual behavior dynamics is complex and depends on an array of factors, including risk perception and disease knowledge and awareness. According to a survey conducted by SSRS for the Annenberg Public Policy Center of the University of Pennsylvania,[45] sampling a nationally representative panel of 1580 USA adults in the period July 12 to 18, 2022, 19% of respondents were worried about contracting monkeypox over the next 3 months. Most of these individuals are uncertain/unsure about how human monkeypox is transmitted and whether it is vaccine-preventable. According to another recent online survey[46] among American gay, bisexual, and other MSM, carried out during August 5 to 15, 2022, participants reported changing their sexual behavior because of the ongoing monkeypox outbreak: 48% reduced their number of sex partners, 50% decreased one-time sexual encounters, and 50% reduced sexual intercourse with casual partners met on dating apps or at sex venues.

In STDs/STIs, sexual behavior dynamics is of paramount importance[47]: heterogeneity in sexual behavior (sex acts and practices, sex partner numbers, anonymous/casual sex partners, mixing pattern or sexual contact, etc.)[48] can, indeed, determine how individual variations impact epidemic patterns, the spread, and the persistence of infection within a specific group (such as the MSM community) and the general population.

After an initial decline, the recent surge in STDs/STIs, especially in the high-risk population, is due to several concurring factors, including the disruptive impact of the still ongoing "Coronavirus Disease 2019" (COVID-19) pandemic on the allocation of funding for sexual health clinics providing free-of-charge STD/STI testing, treatment, and management, the burgeoning of online dating apps and services that have expanded sexual networks, and a significant reduction in condom usage among MSM on HIV PrEP or PEP.[49] Of note, adaptive changes in sexual behavior have been reported in previous outbreaks, including COVID-19, to a varying degree and extent.[50]

Our sexual behavior-related findings are in line with those reported by Brand et al.,[15] who devised a stochastic discrete-population transmission model and found a behavioral-driven decrease in the transmission rate of subjects infected with human monkeypox in the United Kingdom, leading to case incidence flattening and declining over the medium-term forecasts (a 12-week projection period).

We found that, in the scenario of control policies and in the absence of risk compensation, the policies geared toward the use of condoms or sexual abstinence were effective in controlling the current monkeypox outbreak. In addition, a combination of both strategies is more effective than each of the strategies carried out separately. In the presence of risk compensation, the choice of which of the two strategies to implement was strongly reduced, impacting and limiting the freedom to self-regulate and adjust sexual behaviors, with the only effective option to control monkeypox transmission being to impose sexual abstinence by at least 35%. To summarize,

comparing the different scenarios, adaptive control was found to be more effective compared to the robust control, where the daily sexual contact number is reduced proportionally and remains as a constant thereafter. In conclusion, the adaptive behavior changes among the high-risk group can impact the outbreak, by significantly shortening the time to epidemic peak, lowering the epidemic peak size, and facilitating the attenuation of the disease, as such playing a key role in controlling the current outbreak of monkeypox in Canada (Figure 7).

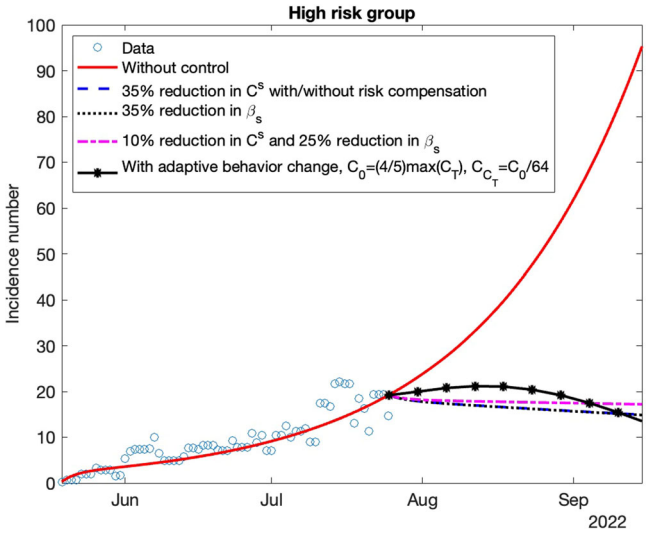

FIGURE 7 Comparison between the model with and without behavior changes.

Our study has several strengths, including the good data fitting, a thorough analysis of sexual behaviors in line with recently conducted surveys on sexual practices and mixing patterns during the monkeypox outbreak and a good estimate of the monkeypox reproduction number of 1.46. These results agree well with the findings of Du et al.,[51] who computed the human monkeypox reproduction number as 1.29 (95% CrI: 1.26–1.33) by aggregating cases from 70 countries from the onset of the outbreak until July 22, 2022 (Figures 8 and 9).

A number of mathematical models have been devised to shed light on the current monkeypox transmission dynamics. Betti et al.[52] developed a new modeling framework that incorporates a modified standard SIR model and pair formation structure with recovery. They show that this model can outperform the standard models with recovery. This model enables the prediction of infectious waves that are not normally observed in standard SIR models: in terms of public health policies, this seems to suggest that particular attention is required to control the outbreak. The authors were also able to estimate the reproduction number for their model to be 2.31–2.66, which is, however, higher than our estimate and the value obtained by Du et al.[51]

Chitwood et al.[53] devised a model focusing on the high-risk MSM population. The authors found that a robust public health response consisting of non-pharmaceutical interventions (i.e., testing and contact tracing) can be effective if at least 40% of human monkeypox cases are detected through community testing, and at least half of case contacts are traced. If the implementation of the package of public health interventions is not vigorous enough (in the scenario of only 10% community detection, and no contact tracing),

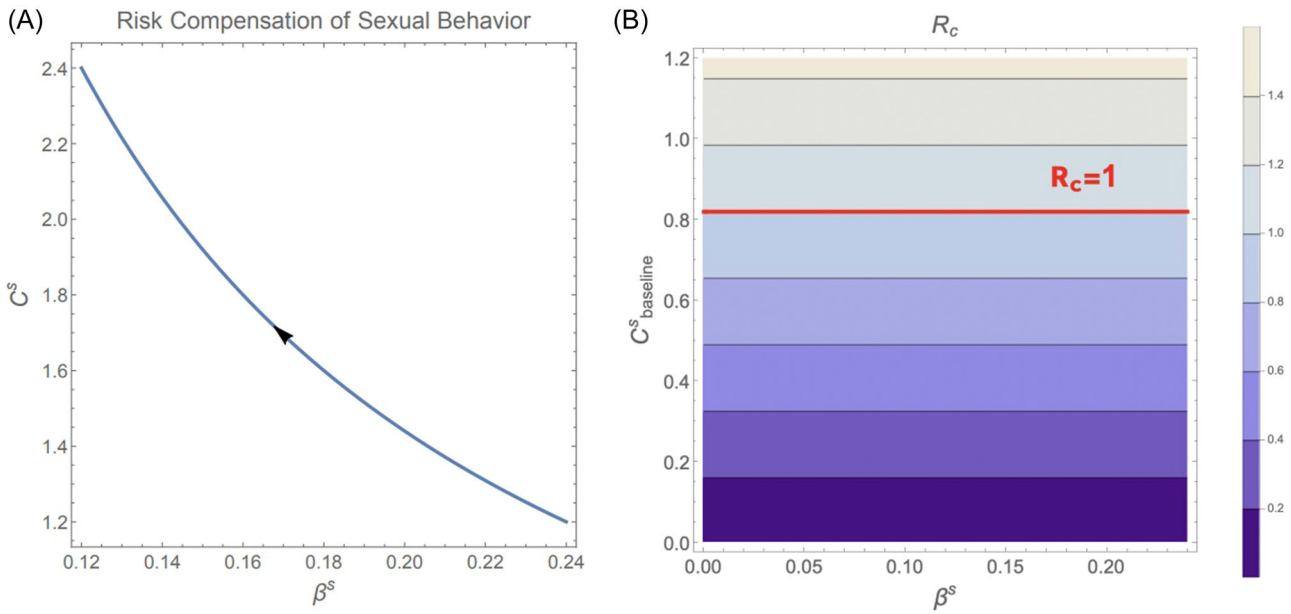

FIGURE 8 Controls with risk compensation behavior change. (A) Relationship between sexual activity level (Cs) and the transmission probability of monkeypox via sexual contact (βs) when risk compensation behavioral change is assumed. (B) Contour plot of the control reproduction number (Rc) with respect to the sexual transmission probability of monkeypox (βs) and baseline sexual contact rate (Cs baseline).

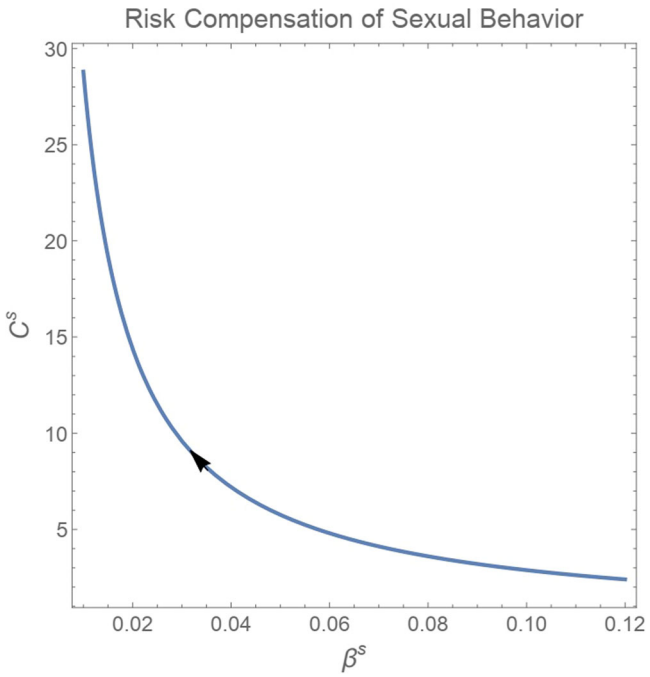

FIGURE 9 Relationship between sexual activity level (Cs) and the transmission probability of monkeypox via sexual contact (βs) near small βs values when risk compensation behavioral change is assumed.

pharmacological interventions (i.e., vaccination) are needed, targeting at least 12%–47% of the MSM population. In the scenario where at least 20% of community cases were detected and at least 25% of cases contact were traced, the critical threshold to vaccinate is reduced to 5%–43% of the population. Yuan et al.[24] reached similar conclusions. The authors devised their model based on the "one health approach," with a human population and an animal reservoir population. The risk of outbreak was found to be greatly reduced if at least 65% of symptomatic cases could be isolated and their contacts effectively traced and quarantined.

The present model does not incorporate monkeypox case under-reporting/underestimation, which may play a role as found in a stochastic modeling study by Ko et al.[54] and in a network modeling study by Van Dijck et al.[55] Even though monkeypox symptoms are visible, a few asymptomatic individuals have been described. A study conducted at a Belgian sexual health clinic[56] found four undiagnosed monkeypox infections out of 224 men previously screened for gonorrhea and chlamydia. Three of these men were completely free of any clinical sign/symptom. Moreover, there are good reasons to suspect under-reporting/underestimation just by looking at data, since, as noted by Nuzzo et al.,[57] the USA, despite having a larger population size, have reported fewer cases than the UK. Moreover, health-seeking behaviors are complex and multi-dimensional, depending on an array of factors, including "predisposing factors" (such as age, sex/gender, ethnicity, or cultural and social variables), "enabling factors" (like financial variables, insurance coverage, or healthcare accessibility/availability), and "need factors" (health, risk, and disease perceptions, medical conditions, or underlying comorbidities).

Symptoms are generally mild and individuals may not seek for healthcare. Furthermore, they are atypical and physicians may not recognize them as monkeypox. A recent knowledge, attitudes and practices (KAP) survey among Italian physicians showed unsatisfying monkeypox-related knowledge levels.[58] Another factor that could result in under-reporting is testing capacity, with a lack of point-of-care tests currently available.[57] Testing and diagnostic capacity is further strained by the still ongoing COVID-19 pandemic. Services and healthcare provisions offered by sexual health clinics in some countries, like the UK, are being significantly impacted and disrupted. This could result in a significant delay with which cases are diagnosed, treated, and reported.

Furthermore, STDs/STIs are highly stigmatized and this could contribute to under-reporting too, even though it is unlikely this may have had an impact on monkeypox case reporting in Canada, given its high score on the LGBT equality index (90 out of 100). Potentially, any sexually active individual could contract the infection, even if the focus is mainly on the MSM community. This could lead to an underestimation of the infectious transmission among other populations. We incorporated close contact/sexual transmission and nonsexual routes only. There could be multiple transmission chains, but data is still scarce and, at least partially, contrasting.

Moreover, even though we captured the main population currently affected by monkeypox in Canada, we did not include other populations (healthcare workers, households, travelers), for which the risk of contracting the infection is negligible (low-risk populations). We also chose not to include some specific populations, like the children, for which there still exist gaps in knowledge.[59,60] Finally, future models should incorporate vaccination and assess other types of sexual behavioral changes, previously described. They should as well investigate the role of other STDs/STIs, such as HIV,[61] in the transmission of monkeypox.

AUTHOR CONTRIBUTIONS

Nicola L. Bragazzi conceived, drafted, and revised the paper. Nicola L. Bragazzi, Qing Han, Sarafa A. Iyaniwura, Xiaoying Wang, Woldegebriel A. Woldegerima, and Jude D. Kong formulated the model, performed data fitting, and conducted simulations. Andrew Omame and Aminath Shausan critically revised the paper. Jude D. Kong and Jianhong Wu supervised the study.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data used for our study is publicly available and can be obtained from Our World in Data [33].

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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