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Exploring the dynamics of the 2022 mpox outbreak in Canada

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Abstract

The 2022 mpox outbreak predominantly impacted gay, bisexual, and other men who have sex with men (gbMSM). Two models were developed to support situational awareness and management decisions in Canada. A compartmental model characterized epidemic drivers at national/provincial levels, while an agent-based model (ABM) assessed municipal-level impacts of vaccination. The models were parameterized and calibrated using empirical case and vaccination data between 2022 and 2023. The compartmental model explored: (1) the epidemic trajectory through community transmission, (2) the potential for transmission among non-gbMSM, and (3) impacts of vaccination and the proportion of gbMSM contributing to disease transmission. The ABM incorporated sexual-contact data and modeled: (1) effects of vaccine uptake on disease dynamics, and (2) impacts of case importation on outbreak resurgence. The calibrated, compartmental model followed the trajectory of the epidemic, which peaked in July 2022, and died out in December 2022. Most cases occurred among gbMSM, and epidemic trajectories were not consistent with sustained transmission among non-

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gbMSM. The ABM suggested that unprioritized vaccination strategies could increase the outbreak size by 47%, and that consistent importation (≥5 cases per 10 000) is necessary for outbreak resurgence. These models can inform time-sensitive situational awareness and policy decisions for similar future outbreaks.

KEYWORDS
agent-based model, Canada, compartmental model, mathematical model, mpox, pandemic

1 | INTRODUCTION

Mpox is caused by an orthopox virus transmitted from wild rodent reservoirs and has long been recognized as a zoonosis. The virus typically results in sporadic self-contained outbreaks among humans in endemic zones in West and Central Africa,[1] with limited human-to-human transmission.[2] While occasional global spread due to travel-related infections has previously occured,[3] the 2022 mpox outbreak[4] was unprecedented for two reasons. First, the global spread was unparalleled: mpox was first reported in the United Kingdom in May 2022 in a traveler arriving from Nigeria,[5] but subsequently spread to over 110 countries by October of 2023, with over 90 000 cases reported globally.[6] Second, the global epidemic was associated with sexual transmission amongst gay, bisexual, and other men who have sex with men (gbMSM), previously unseen.[7]

In Canada, the first mpox case was detected at the end of April 2022 in the province of Quebec. Although cases were subsequently reported in all other provinces, they were concentrated in British Columbia (202 cases; population 5.3 M), Ontario (722 cases; population 15 M), and Quebec (533 cases; population 8.7 M).[8–10] The national epidemic peaked in July 2022 (~30 cases/day), culminating in 1515 cumulative cases as of October 2023.[9] As elsewhere in the world, gbMSM were predominantly affected, representing >99% (1500/1515) of cases in Canada. Throughout the epidemic, the Government of Canada advised practicing safer sex (condoms), decreasing the number of sex partners, and limiting sexual and close physical contact with individuals with infectious lesions.[11,12] On June 8, 2022, Canada's National Advisory Committee on Immunization authorized the use of the Imvamune vaccine for both pre and postexposure prophylaxis against mpox infection.[13]

The largely sexual nature of disease transmission combined with uncertainty of vaccine effectiveness[14] resulted in ambiguity regarding the epidemic trajectory, its drivers, and the impacts of interventions on the outbreak. Here we used two complementary modeling approaches that were developed to support situational awareness and public health responses in Canada. The first approach, a compartmental model, was used to: (a) project the national/provincial outbreak trajectories under various scenarios, (b) explore the likelihood of wider community transmission in the population, and c) characterize the impact of vaccination. The second approach uses an agent-based model (ABM) to explore hypothetical vaccination scenarios at a municipal level, and the role of case importation for outbreak resurgence.

2 | METHODS

Both the compartmental model and ABM implemented a susceptible-exposed-infectious-recovered (SEIR) structure incorporating various data sources. The compartmental model was fit to reported cases at both the national and provincial levels (for British Columbia, Ontario, and Quebec), while the ABM incorporated a population-level sexual contact network, and was fit to Quebec-level case data, where the first mpox case in Canada was reported. The model formulation and parameterization are summarized below. Both models were coded in R, version 4.1.2.[15]

2.1 | Data

The models were parameterized using publicly available data on daily mpox cases in Canada, stratified by age, sex, and province[9] from April to December of 2022. Vaccination data for June–December 2022 were collected by the Public Health Agency of Canada with weekly reporting by most provinces. In addition, the ABM was informed using data collected during the baseline visit (February 2017–June 2018) of the Engage Cohort Study–a longitudinal study collecting sexual behavior data from gbMSM (including transgender men) recruited using respondent-driven sampling on the Island of Montreal.[16]

2.2 | Compartmental model

2.2.1 | Model structure

The model was developed in the R package "McMasterPandemic"[17]–a compartmental epidemic model builder for forecasting and analysis of infectious disease epidemics, in preparation for generic pandemic response during the COVID-19 pandemic to explore the community spread of emerging pathogens in Canada.[17] The model was calibrated independently to the national and provincial case counts. Since most mpox cases were reported among gbMSM, who represent on average, 1%–3% of the Canadian population,[18,19] 1.5%[20] of the model population was stratified as gbMSM. To account for population-level heterogeneity among gbMSM,[21] 50% of gbMSM were assumed to be within the "effective" population, that is, representing a subgroup that may be more likely to acquire mpox infection.

The model was stratified into four groups reflecting population heterogeneity and vaccination status:

1. gbMSM; unvaccinated.
2. gbMSM; vaccinated.
3. Non-gbMSM; unvaccinated.
4. Non-gbMSM; vaccinated.

Each group contains its own epidemiological (SEIR) compartments and parameters (Table 1 and Supporting Information Table S1), along with a probability matrix describing both inter (i.e., between group mixing) and intragroup mixing (homogenous within group). The modeled population was assumed to be unvaccinated until June 2022, when vaccines became available. Vaccination was implemented in the model by computing a moving daily vaccination rate for each reporting week. For simplicity, it was assumed that mixing patterns did not vary by vaccination status, thus reducing the probability mixing matrix to a 2 by 2 matrix.

2.2.2 | Force of infection

The time-varying force of infection (FOI) for the vaccinated (v) and unvaccinated (u) groups ($f = 1, 2$ representing gbMSM and non-gbMSM, respectively) was calculated as follows:

$$FOI(t)_{f_1 u} = \frac{P_{f_1}\beta_{f_1}(t)I_{f_1}}{N_{f_1}} + \frac{P_{f_1 f_2}\beta_{f_1}(t)I_{f_2}}{N_{f_2}}, \quad (1)$$

$$FOI(t)_{f_1 v} = (1 - VE) \times \frac{P_{f_1}\beta_{f_1}(t)I_{f_1}}{N_{f_1}} + (1 - VE) \times \frac{P_{f_1 f_2}\beta_{f_1}(t)I_{f_2}}{N_{f_2}}, \quad (2)$$

where VE is the vaccine effectiveness; $\beta_{f_1}(t)$ represents the time-varying transmission rate; I_f is the number of infectious individuals in group f; N_{f_1} is the effective population size of gbMSM; $N_{f_2}$is the population size of non-gbMSM, and P is the group-level probability of mixing defined in the group mixing matrix where the elements are as follows:

$$P_{f_1 f_2} = \frac{P_{f_2 f_1}(1 - Prop_{eff}Prop_1)}{Prop_{eff}Prop_1}, \quad (3)$$

$$P_{f_1} = 1 - P_{f_1 f_2}, \quad (4)$$

$$P_{f_2} = 1 - P_{f_2 f_1}. \quad (5)$$

where $P_{f_2 f_1}$ is assumed to be 0.0005. This formulation accounts for the difference in the population size of gbMSM and non-gbMSM.

A similar formulation applies to the FOI for $f = 2$ (i.e., non-gbMSM) where $\beta_{f_2} = \beta_{f_1}\beta_{factor}$ The model allows for time-varying, piecewise changes in the transmission rate ($\beta(t)$) due to behavior change and nonpharmaceutical interventions. The piecewise change in transmission rate occurred at the time best capturing the moment of the epidemic turnover (Supporting Information Table S1).

2.2.3 | Model calibration

The trajectories were calibrated to the surveillance time-series of reported cases at the tajjsgfasfnational and provincial levels independently. This was accomplished by simulating a deterministic instance of the model using an initial set of parameters and then calculating and maximizing the respective log-likelihood. The surveillance data were assumed to be independently distributed under a negative binomial distribution with a dispersion parameter. The initial and time varying transmission parameters were optimized using the Nelder-Mead algorithm of R's built-in "optim" function.[25]

2.2.4 | Model simulations

The calibrated model was used to explore the impact of model parameters (e.g., effective population size, vaccine effectiveness, mixing between, and transmission within and between groups), affected

TABLE 1 Table of parameters used in the compartmental model of mpox transmission dynamics in Canada (2022–2023).

Parameter	Value	Meaning	Reference
$Prop_1$	0.015	gbMSM proportion	[20]
α	7 days	Time in exposed class	[22]
γ	14 days	Time from infection to recovery	[23]
β_{factor}	1/8	Transmission scaling factor for non-gbMSM	Assumed
Reporting fraction	0.8	Reporting fraction	Assumed
CV reporting delay	2	Coefficient of variation for reporting delay	Assumed
Mean reporting delay	5 days	Mean reporting delay	Assumed
VE	0.85	Vaccine effectiveness	[24]
$Prop_{eff}$	0.5	Effective proportion of gbMSM	Assumed
δ_1	1/5	Over dispersion for negative binomial gbMSM observation error	Assumed
δ_2	1/50	Over dispersion for negative binomial non-gbMSM observation error	Assumed

epidemic dynamics, and the consistency of model outputs with the observed epidemic. Prediction intervals of trajectories were based on 200 multivariate normal samples of the calibrated parameters and simulating a negative binomially distributed stochastic trajectory for each sample from the model. The 2.5%, 97.5%, and 50% quantiles of these 200 stochastic trajectories were used as prediction intervals and medians respectively.

Scenario matching simulations

Three scenarios were modeled weekly during the epidemic (in real-time) and were then compared against observed cases reported the following week. Only the set of simulations, conducted at the end of August 2022 are shown. Vaccine rollout was included in all scenarios. In the first scenario, the calibrated model, which assumed an effective proportion of the gbMSM population of 50% and an individual-level vaccine effectiveness of 85%,[24] was used to fit the status quo epidemic trajectory using the calibrated transmission rates. Two counterfactual scenarios in which the time-varying transmission parameter was varied were considered for each jurisdiction and compared to the status quo epidemic trajectory:

1. Uncontrolled outbreak; no change to the transmission rate due to non-pharmaceutical interventions.
2. Partially controlled outbreak; reduced transmission rate such that the effective reproduction rate (R_t), which is the average number of secondary infections from an index case at time t, is close to 1.

Impact of mixing and transmission among and between groups

Although most cases were reported among gbMSM, there remains a potential for transmission into and amongst the non-gbMSM group. To explore the likelihood of this, the transmission rates within the non-gbMSM group and the intergroup mixing probabilities among gbMSM were varied. In the status quo scenario, a low transmission rate and intergroup mixing probability were assumed for the non-gbMSM population. Alternative scenarios simulated all combinations of low (0.0005; 1/8), medium (0.001; 1/4), and high (0.002; 1) levels of the probability of mixing between non-gbMSM and gbMSM and scaling factor for transmission amongst non-gbMSM respectively. Medium and high transmission rates and probabilities were chosen after determining the status quo scenario.

Vaccine effectiveness and the effective proportion of gbMSM

The size of the outbreak and prioritized intervention strategies was assessed by varying the effective proportion (20%, 50%, and 80%) of gbMSM. Given uncertainty in the vaccine effectiveness, three estimates (0%, 40%, and 85%) were considered. It was assumed that individuals received one vaccine dose during the model simulation and subsequently completed the vaccine course to maintain effectiveness.

2.3 | ABM

The ABM was used to test hypothetical vaccination scenarios in the absence of behavior change. The model simulates a population of 10 000 gbMSM aged 15+ years living on the island of Montreal, Quebec. The model, which is described in detail in Milwid et al.,[21] includes dynamic partnership formation, partnership dissolution, population demographics, and disease transmission processes. In contrast to the original model which simulated HIV transmission through anal sex, the current model simulates mpox transmission through any sexual acts (i.e., mutual masturbation, oral, anilingus, frontal, and anal sex acts).

2.3.1 | Partnership formation

Upon entry into the model, men were assigned an age-varying, annual number of sex partners using a negative binomial distribution (mean = 3.33, dispersion parameter = 0.28; Supporting Information Table S2). As in Milwid et al.,[20] the annual partner change rate was used to determine each man's weekly partnership quota, with partnerships forming based on age preference. The partner change rate was calculated based on the following *Engage Cohort survey* question:

> *"During the past 6 months, with how many guys have you had any kind of sex (anal, oral, mutual masturbation, rimming, frontal/vaginal, etc.)"*

Partnerships were classified as *casual or regular* (with the latter representing 40% of partnerships).[21] As in [21], casual partnerships were assumed to start and end within the same week, and were randomly assigned 1–3 sex acts. Conversely, the duration of regular partnerships, informed by *Engage Cohort Survey* data, was assumed to exceed 1 month. The per-partnership number of sex acts for regular partnerships followed a Poisson distribution ($\lambda = 4.12$) and was informed by the following question:

> "How many times have you had any kind of sex with the [regular] partner named above in the past *6 months?"*

2.3.2 | Vaccination

Routine smallpox vaccination was discontinued in Canada in 1972.[26] Waning of vaccine-induced immunity among older cohorts may have contributed to the current mpox resurgence,[24] and the extent of protection from childhood vaccination is unclear. Therefore, the proportion of men aged 50+ years with vaccine-induced protection against infection was estimated during the model fitting process.

Recent vaccination events were assumed to confer life-long immunity, and were modeled in accordance with the estimated weekly uptake rate in Quebec. Preliminary data from Statistics Quebec approximates 851 593 males on the island of Montreal aged 15+ years in 2022.[27] It was assumed that gbMSM represent 6.4% of the male population,[21] resulting in approximately 54 500 gbMSM in

Montreal. The proportion of men vaccinated each week was estimated from province-level vaccination records. The vaccination data represent a count of all men vaccinated in Quebec, including travelers and health care professionals, and may over-represent the city-level uptake.

The estimated weekly vaccination rate was used to randomly sample eligible men. The simulated eligibility criteria mirrored the evolving provincial level guidelines: gbMSM were eligible for vaccination if they: (a) had contact with an infected person (May 30, 2022–June 2, 2022), (b) had ≥2 sex partners in the past 2 weeks or had direct contact with an infected person (June 3, 2022–June 14, 2022), and (c) had >1 regular partner (June 14, 2022 onwards).[28,29] In the model, men received one dose of the mpox vaccine, which was assumed to confer 85% protection from infection[24] 2 weeks after vaccination. The vaccine was assumed to have no impact when administered to men who already acquired mpox.

2.3.3 | Mpox transmission

Given uncertainty surrounding the date and number of imported cases into Canada, the estimated date of importation (March–April 2022) and the number of imported cases (1–3) were calibrated during the fitting process. All imported cases were assumed to be in the exposed disease state, to have >10 annual sexual partners, and be younger than 50 years.

Disease transmission between susceptible and infectious partners was simulated using a Bernoulli process, taking the susceptible partner's vaccination status into account (Equation 6). Upon acquiring infection with mpox, the person transitioned to an *exposed* state (duration: 5–21 days),[22] followed by an *infectious* state (duration: 2–4 weeks),[23] and finally *recovered* with lifelong immunity. A Bernoulli distribution was used to determine when each man transitioned between stages. Accordingly, all transition rates were converted to probabilities.

$$P = 1 - (1 - Prob\_transmission^{*}(1 - VE))^{n\_sex\_acts}, \quad (6)$$

here VE represents the vaccine effectiveness (VE = 0% or 85% for unvaccinated and vaccinated individuals respectively). Furthermore, *n_sex_acts* is the number of sex acts per timestep within the partnership.

2.3.4 | Model calibration

An approximate Bayesian computation-sequential Monte Carlo fitting technique was used to calibrate the model to the weekly number of confirmed and probable cases, from May to August 14, 2022. While the natural history of mpox (Section 2.3-3) was used to inform the model priors, uninformative priors were used to estimate the remaining parameters. The model calibration produced 100 unique parameter sets which resulted in good fits (Supporting Information Figure S1).

2.3.5 | Model simulations

Impact of vaccine uptake

In the baseline scenario, the reported uptake rate for the first vaccine dose between July and December 11, 2022 was implemented in the model, with the last reported uptake rate remaining constant for the remainder of the year. Starting in January 2023, no further vaccination was simulated. The impact of prioritized vaccination was assessed by comparing simulations in which men with at least 1, 2, or 5 annual sexual partners could be vaccinated. To test the effect of vaccination in the absence of behavior change and of the potential overestimation in the reported vaccine uptake, scenarios were simulated in which there was a 10, 25, 50, 75, and 100% decrease in the estimated uptake rate. Additional scenarios included simulating the estimated vaccination rate until the first of week of August 2022, after which it decreased linearly to 0% by the last week of September, October, November, and December.

Characterizing the potential for an mpox resurgence

The potential for an mpox resurgence was assessed by simulating case importation into Montreal from January 2023 onwards, assuming no further vaccine distribution after December 11, 2022. Two scenarios were modeled in which imported cases: (a) remained constant at 1, 5, 10, or 15 cases per 10 000 week^{-1}, and (b) varied in accordance with estimates produced by a mpox importation model (unpublished). Briefly, the importation model is a statistical model combining travel volume into Canada with the global mpox incidence to estimate the weekly number of cases imported into Canada. In the current work, the importation estimates were scaled to the modeled population of 10 000 agents. As it was assumed that all cases were imported into Montreal, the importation estimates likely over-represent the imported cases, and were scaled by factors of 0.5, 1.5, and 2 to explore a range of scenarios (Supporting Information Figure S2A). The imported cases were assigned an age proportional to the age distribution of cases in Montreal (Supporting Information Figure S2B) AND AN *exposed* disease status. The cumulative proportion of incident cases was calculated for each scenario, excluding the imported cases themselves.

Each scenario was simulated between May 2022–December 2023 using all 100 parameter sets with 50 seeds. The median of the resulting number of weekly incident cases was calculated and scaled to the daily resolution, and the estimated gbMSM population size for Montreal. The 95% credible intervals (CrI) were computed.

3 | RESULTS

3.1 | Compartmental model

3.1.1 | Epidemic characteristics

The status quo fit was used to track the progression of the outbreak; calibrated transmissions rates for all jurisdictions are in Supporting Information Table S1. At the national level, cases peaked in mid–July (30 cases/day; CI: 10–45), and decreased thereafter, reaching zero cases

between September and December 2022. Conversely, incident cases in the uncontrolled growth counterfactual had the potential to increase from May to September 2022, peaking at 4200 (CI: 1500–8100) cases/day until the majority of gbMSM acquired infection. Finally, under the assumption of partial control, the trajectory plateaued in July at 30 (CI: 10–50) cases/day. The uncontrolled scenario diverged from the status quo (tracking the corresponding surveillance data) fit after early June, and the partially controlled scenario after mid-July indicating that the outbreak was coming under control. Similar trends were observed at the provincial level, with Quebec experiencing the earliest epidemic peak. Although the peak times were similar for Ontario and British Columbia, the modeled outbreak size in British Columbia was lower than the other provinces (Figure 1).

3.1.2 | Characterizing the impact of intergroup mixing and transmission

A sensitivity analysis exploring the relationship between intergroup mixing and the transmission rate among non-gbMSM, highlighted the necessity of high transmission rates within that group to facilitate sustained community transmission among non-gbMSM. The empirical case count data (represented by the blacks points in Figure 2) for which >99% of cases were reported among gbMSM, best matched the observed dynamics in which there was low intergroup mixing and a low transmission rate in the non-gbMSM group (Figure 2, bottom-left panel). Interestingly, increasing the intergroup mixing probability resulted in a reduced number of effective transmission events among gbMSM, and, consequently, a lower overall incidence within that group along with a small and insubstantial increase in incidence in the non-gbMSM group. In all scenarios, apart from scenarios in with high transmission levels in the non-gbMSM group combined with medium-high levels of intergroup mixing, the majority of mpox cases were estimated to occur among gbMSM (Figure 2).

3.1.3 | Vaccine effectiveness, uptake, and strategy

In all scenarios (status quo, uncontrolled, and partially controlled), increasing the effective proportion of gbMSM resulted in an increased incidence while increasing the vaccine effectiveness lowered incidence. Adjusting the vaccine effectiveness had a minimal impact when combined with low effective proportions (Figure 3), however, the increase in incidence was more evident as vaccine effectiveness decreased in the counterfactual scenarios. Overall, there was little support from the simulations that vaccination was a major factor that resulted in control of the mpox outbreak in Canada given the low vaccine coverage and rollout when incidence had peaked and was decreasing.

3.2 | ABM

3.2.1 | Impact of vaccine uptake in the absence of behavior change

In the baseline scenario, similar characteristics were simulated to those projected for Quebec using the compartmental model (epidemic peak: end of June 2022; 5 cases/day, 95% CrI: 3–9

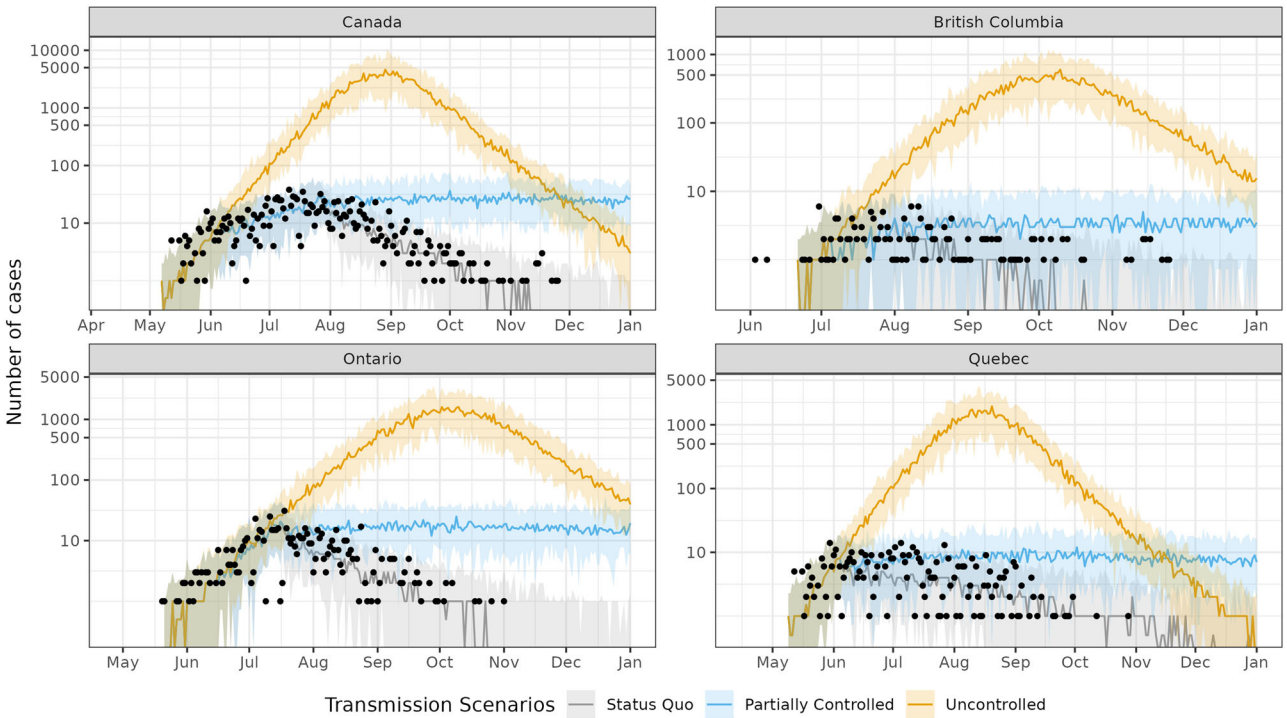

FIGURE 1 Simulated trajectories of the 2022 mpox outbreak using a compartmental model for Canada nationally, and the provinces of British Columbia, Ontario and Quebec. Three scenarios were generated: (1) the status quo (gray curve), (2) uncontrolled epidemic growth with constant transmission rate (orange curve), and (3) partially controlled epidemic growth (blue curve); the black points represent the daily reported cases from Canada's national mpox surveillance.

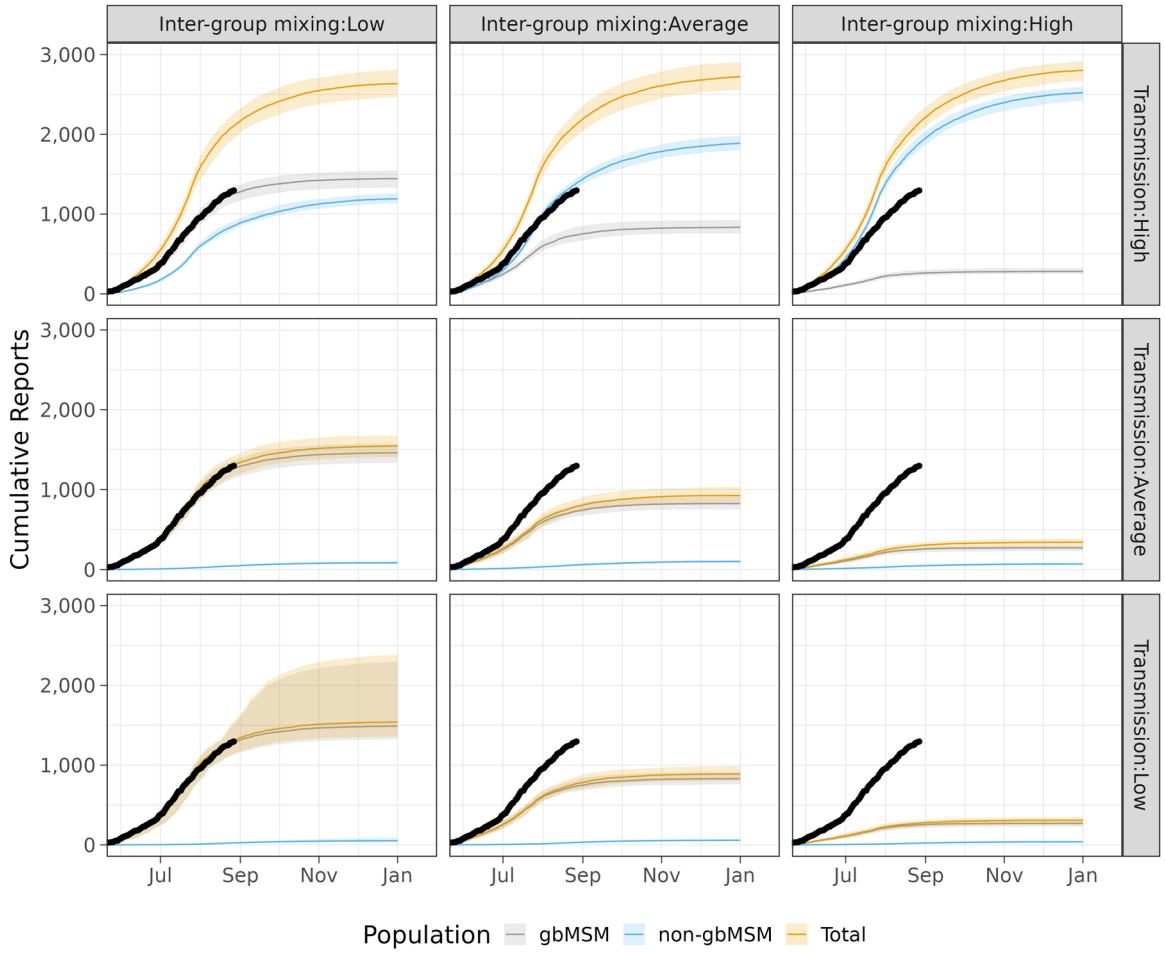

FIGURE 2 Simulated cases of mpox among gbMSM (represented with the gray curve) and non-gbMSM (represented with the blue curve) over time. Three scenarios for intergroup mixing probabilities (low, average, and high; represented by the columns) and transmission rates within the non-gbMSM community (low, average, and high; represented by the rows) were simulated. Empirical data are represented by the black points, and describe the cumulative case counts observed from the national mpox surveillance during the specified time period.

cases/day). While tightening the vaccination eligibility criteria to men with ≥5 annual sexual partners had minimal impact on the epidemic trajectory, widening the eligibility criteria to men with ≥1 annual sexual partner was expected to increase infections in 2022 on average by 47% (CrI: −27%–182%), this result had high uncertainty. Furthermore, a delayed epidemic peak that shifted from June to mid-July was simulated but not observed in the empirical data (Figure 3B).

Compared to the baseline scenario, in which the reported vaccine uptake was assumed to be distributed to gbMSM in Montreal, the epidemic peak shifted from the end of June to: mid-July (7 cases/day; CrI: 1–16 cases/day), early August (6 cases/day; CrI: 1–19 cases/day), late August (9 cases/day; CrI: 1–29 cases/day), mid December (21 cases/day; CrI: 1–69 cases/day) and mid December (46 cases/day; CrI: 5–116 cases/day) when the proportion vaccinated was decreased by 10%, 25%, 50%, 75%, and 100% respectively (Figure 4A). Minimal changes to the epidemic trajectory were observed when linearly decreasing the vaccine coverage to 0% starting in August 2022 (Figure 4B).

Consistent case importation was necessary to invoke a sustained mpox resurgence. When ≥5 cases per 10 000 were imported weekly, the epidemic experienced a growth in incidence resulting from onward community transmission, particularly in the high sexual activity group (men with >10 annual sexual partners) of which up to 10% acquired infection by the end of 2023. Less than 5% of the low and medium (<5 and 6–10 annual sexual partners, respectively) sexual activity groups is expected to acquire infection in the case of an epidemic resurgence. Conversely, in the event of a short burst of imported cases, there was a brief delay in local transmission, with incidence increasing in April 2023. The local dynamics mirrored those of the original outbreak, with the high sexual activity group experiencing the largest proportion of incident cases, before decreasing to zero by December 2023 (Figure 5).

4 | DISCUSSION

The 2022 global mpox outbreak raised questions regarding epidemic dynamics and effectiveness of control methods. To explore these complexities in Canada, and support public health decisions, two independent models incorporating mixing and assumptions from the

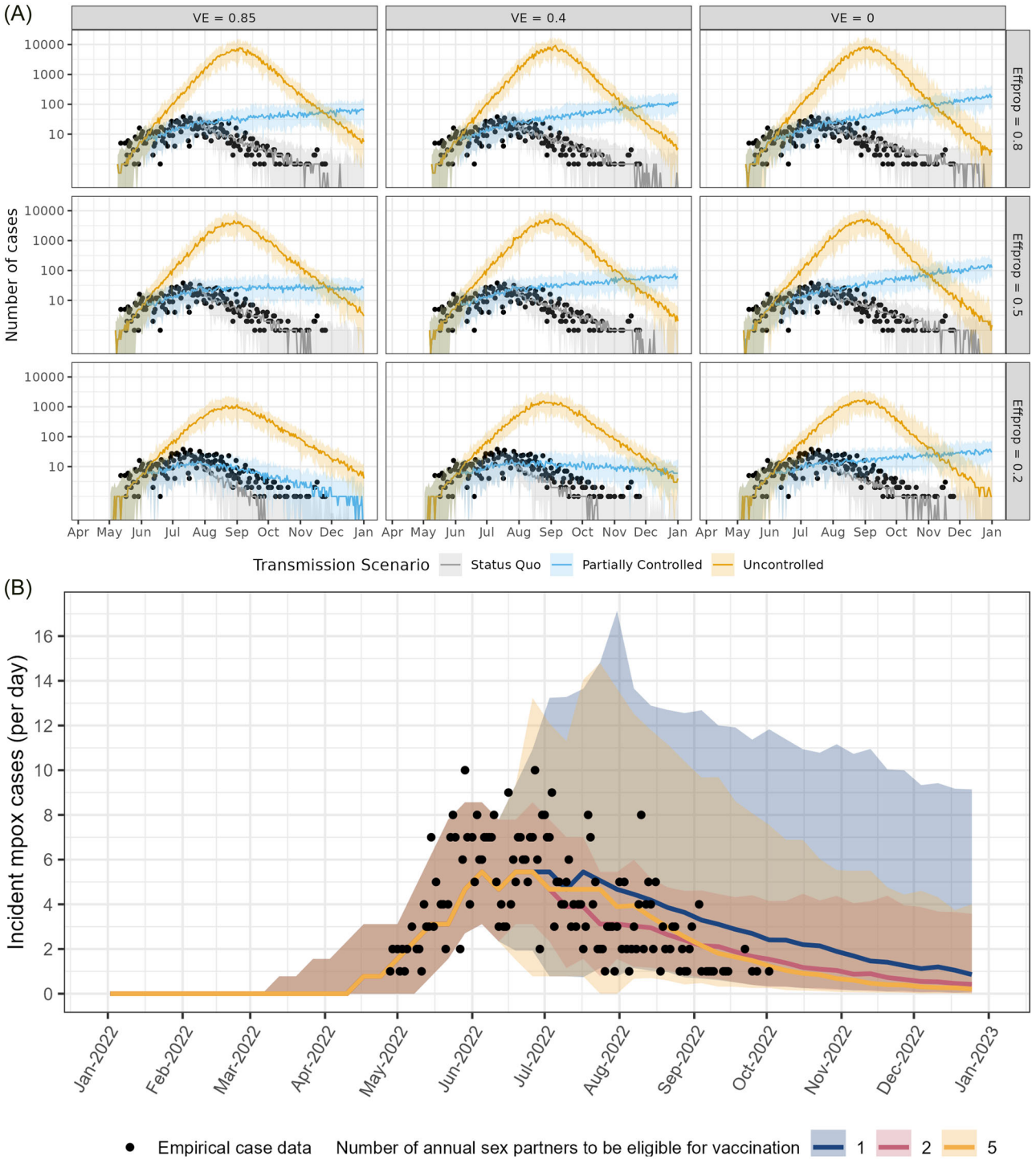

FIGURE 3 Impact of vaccine characteristics and distribution on the epidemic trajectory. (A) Sensitivity analysis performed by a compartmental model, assessing the impact of varying vaccine effectiveness estimates and distribution strategies. Decreasing the vaccine effectiveness, and/or increasing the proportion vaccinated resulted in increased epidemic sizes under the uncontrolled, partially controlled, and status quo scenarios. (B) Results of an agent-based model of mpox transmission among gay, bisexual, and other men who have sex with men in Montreal, Canada. The model results highlight the impact of changing vaccine eligibility from men with ≥2 annual sex partners to men with at least 1 or 5 annual sexual partners. The increased eligibility resulted in an increased epidemic size, while tightening the eligibility criteria had minimal effect on the epidemic trajectory. The solid lines represent the median number of incident cases and the shaded region represents the 95% credible Interval. The black points in both panels represent the empirical case data. Effprop, effective proportion; VE, vaccine effectiveness.

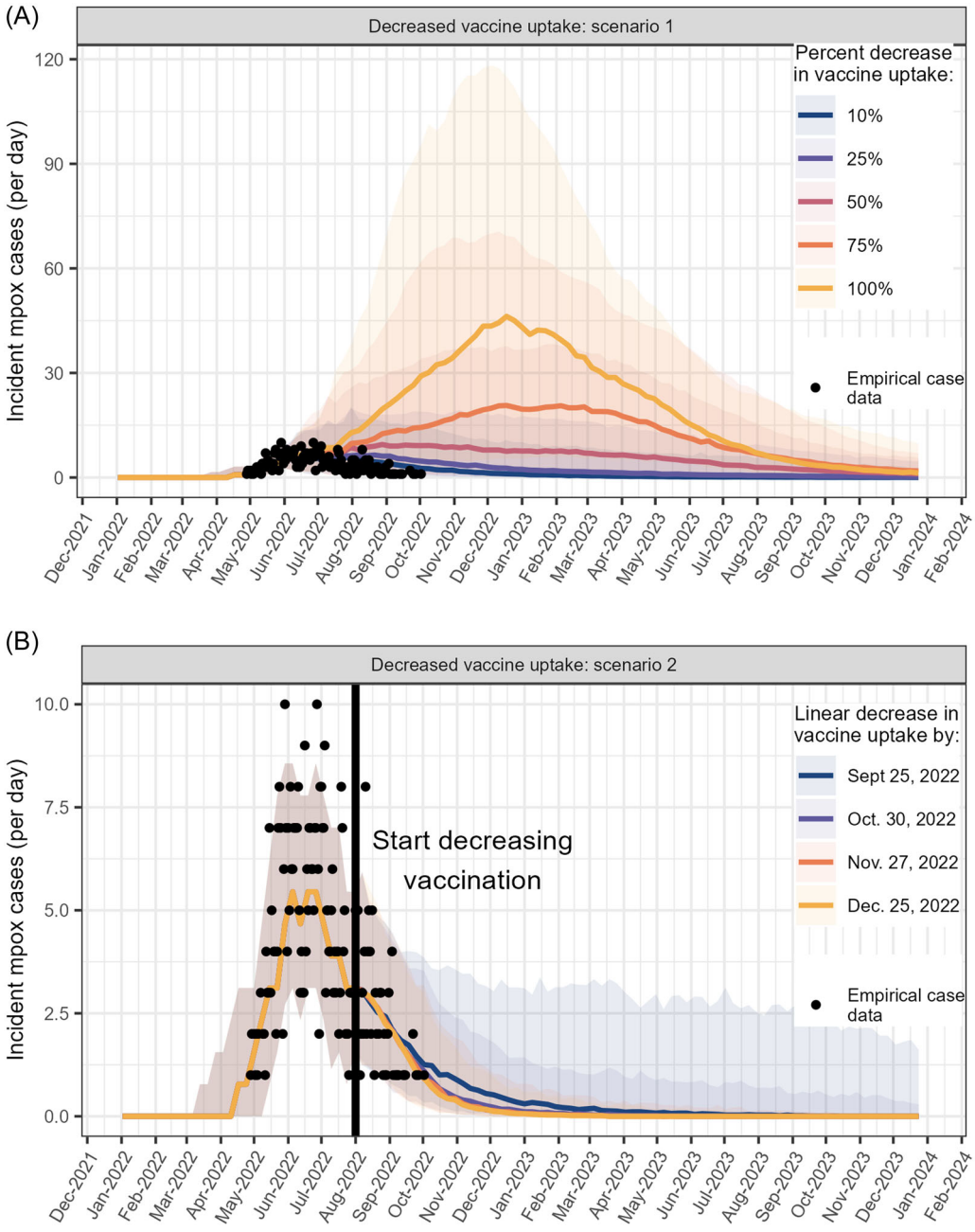

FIGURE 4 Simulated impact of decreased vaccine uptake in Montreal gay, bisexual, and other men who have sex with men, using an agent-based model of mpox transmission. (A) Temporal trends in the mpox incident cases when the estimated vaccine uptake was decreased by 10%, 25%, 50%, 75%, and 100%. The epidemic peak height and time increased when vaccination uptake decreased. (B) Minimal changes in the incident cases were observed when the mpox vaccine uptake decreased linearly, starting at the beginning of August, 2022. The solid line represents the median number of incident cases, and the shaded region represents the 95% credible interval. Case resurgence.

literature on sexually transmitted infections, were adapted and analyzed at the national, provincial, and municipal levels. The compartmental model incorporated assumptions regarding mixing patterns between gbMSM and non-gbMSM to characterize population-level community transmission, while the ABM integrated detailed sexual contact patterns. Model results suggest that: (1) behavior change rather than vaccination was likely the main cause of the short epidemic duration, (2) in the absence of behavior change, vaccination programs can decrease the size and duration of the outbreak, and (3) continued case importation is necessary for a mpox resurgence.

Similarly to Brand et al., (2023) the compartmental model highlighted the contribution of behavior changes to the evolution of the outbreak, including the short epidemic duration.[30] The delayed and greater epidemic peak simulated in the uncontrolled growth scenario, compared to observed cases, suggests that the decreased transmission likely resulted from behavior. Additionally, a sensitivity analysis exploring

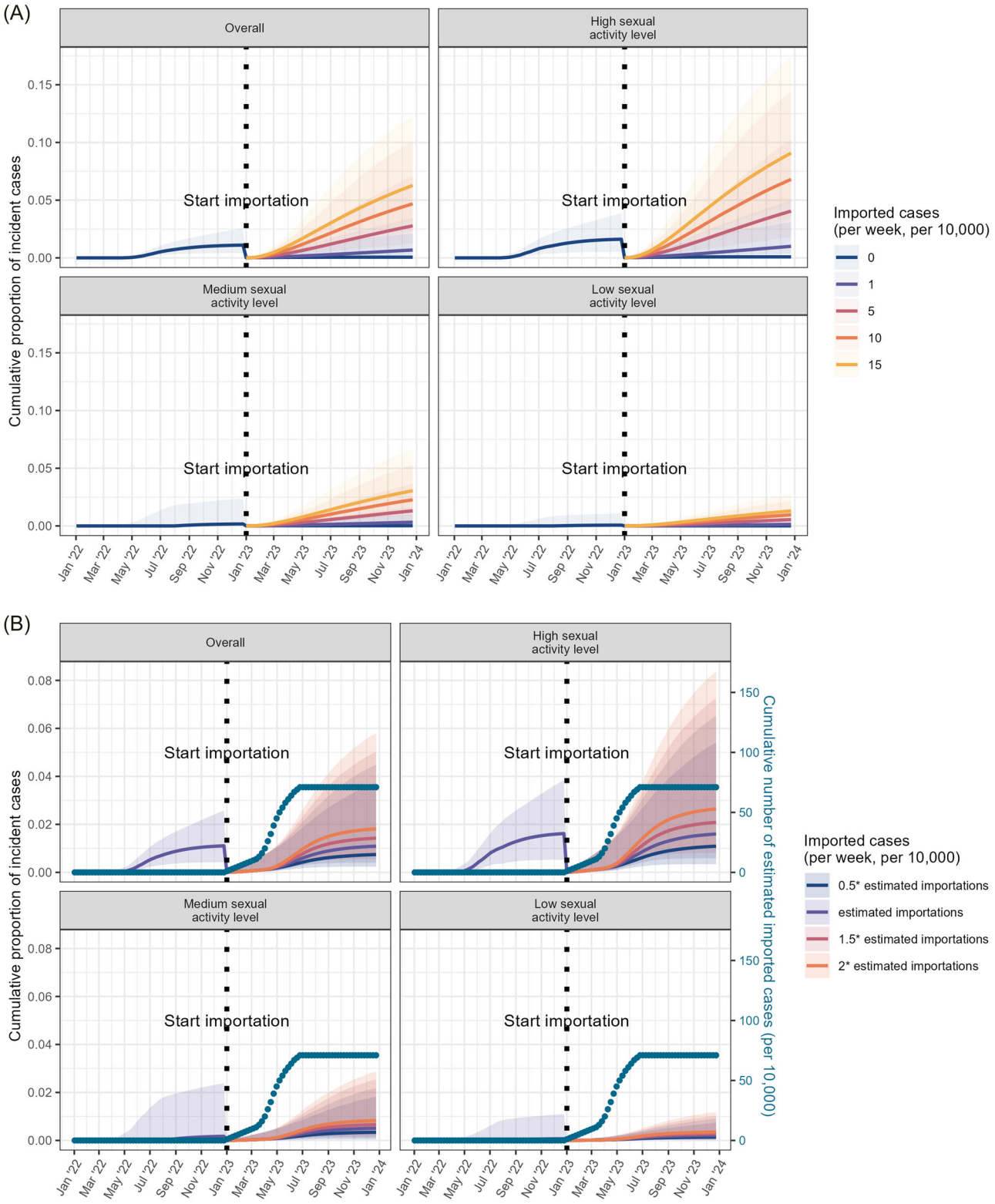

FIGURE 5 Impact of mpox case importation on epidemic resurgence. Cases were imported weekly, starting in in January 2023. The solid lines represent the median number of incident cases in Montreal, and the shaded region represents the 95% credible interval. (A) A scenario in which a consistent number of cases were imported into Montreal each week. (B) A scenario in which cases were imported in accordance with estimates produced by an importation model (unpublished). The cumulative number of cases imported are represented using the blue points (right *y* axis). In both scenarios, the high-sexual activity group (e.g., men with >10 annual sexual partners) experienced the largest proportion of cases, while minimal cases were observed in the low and medium sexual activity groups (e.g., men with <5 and 6–10 annual sexual partners respectively).

vaccine effectiveness and the effective proportion of gbMSM had minimal impact on the status quo trajectory, suggesting that vaccination did not play a large role in the 2022 outbreak. This is consistent with the timing of the vaccine rollout (June 2022)[13] which was close to the epidemic peak. Finally, in accordance with surveillance data,[9] the analysis suggests that the unique mixing structure among gbMSM contributed to the short epidemic duration and size. Furthermore, there was minimal likelihood of sustained mpox transmission among non-gbMSM, which would have resulted in an increased case count and epidemic duration, and supports the strategy used by published studies that model mpox transmission among gbMSM only.[31]

The ABM results suggest that a prioritized vaccination strategy[29] would have a greater impact on reducing incidence. This likely results from the low mpox prevalence,[21] as the random allocation of vaccines in an unprioritized strategy is less likely to effectively reach and protect individuals at higher risk of mpox acquisition. The importance of vaccination strategy was demonstrated by Knight et al., who showed that in situations with limited vaccine availability, vaccination was more beneficial in limiting mpox spread when distributed to individuals with larger networks or those with more initial infections.[32]

Although the national and global mpox incidence has declined,[33] minor outbreaks continue to be reported globally (e.g. in the Western Pacific Region),[33] presenting a risk of importation into, and resurgence within Canada.[34] Corresponding with recent data suggesting small, sporadic, localized outbreaks in Canada,[9] this work highlights the role of global mpox incidence, via case importation, in influencing the likelihood of sustained resurgent outbreaks.[30,34,35] Additionally, increased levels of both vaccine- and infection-induced immunity likely resulted in a growing proportion of the population with protection against future infection, thus impacting the likelihood and outcome of future outbreaks in the short/medium term.[34]

There are inherent limitations within this study. While the compartmental model is simplistic and does not include standard sexual contact patterns[36] typically used in compartmental models of sexually transmitted infections, the purpose was to explore population-level community transmission patterns, especially at the epidemic onset when there were uncertainties regarding the transmission route and minimal surveillance data. Furthermore, the model was used in conjunction with the more detailed ABM, both of which resulted in similar epidemic characteristics. Next, ambiguity in the vaccine effectiveness necessitated assumptions within the models that could have resulted in smaller outbreak projections, however, a sensitivity analysis on the vaccine effectiveness confirmed the feasibility of the effectiveness estimate for the current study and importance of vaccination.[37] Additionally, although the compartmental model highlighted the likely instrumental role of behavioral changes (e.g., reduced number of sex partners, condom use) in the epidemic dynamics, such changes were not included in the ABM due to a paucity of empirical data. Also there is limited evidence on effectiveness of childhood smallpox vaccination (calibrated using uninformative priors), the proportion of asymptomatic cases, and the rate of contact tracing (assumed to be 100%), for which various assumptions were employed in the ABM. Finally, the sexual contact data used to parameterize the ABM were obtained before the SARS-CoV-2 pandemic. Nevertheless, while contact patterns may have changed since data collection, the Engage data represent the most up-do-date source on local contact patterns.

The unprecedented mpox outbreak occurred during the SARS-CoV-2 pandemic, creating a public health challenge globally.[38] While the SARS-CoV-2 pandemic caused a depletion and strain of public health services and resources, the lessons learned from the management of the pandemic resulted in many countries having increased capacity and preparedness to respond to emerging/re-emerging disease outbreaks, including modeling to support public health decisions. The availability and flexibility of the modeling toolset described in this paper provided the immediate capability to inform situational awareness efforts, and to explore the evolving situation. The models highlighted the localized nature of the outbreak, as well as the importance of focused prevention strategies in circumventing similar outbreaks in the future.

AUTHOR CONTRIBUTIONS

Rachael M. Milwid and Michael Li developed the models, conducted the analysis and draft the manuscript. All authors commented and edited to produce the final version.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The national and provincial surveillance data are publicly available at https://health-infobase.canada.ca/mpox/. Additional data that support the findings of this study are available from Engage. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from the author(s) with the permission of Engage.

ETHICS STATEMENT

Ethics approval was not required for this study.

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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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