Title: Maximizing the impact of limited vaccine supply under different early epidemic conditions: a 2-city modelling analysis of monkeypox virus transmission among men who have sex with men

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Abstract

Background. The current global monkeypox virus (MPVX) outbreak has disproportionately affected gay, bisexual, and other men who have sex with men (GBMSM). Given that many jurisdictions have been faced with limited supplies of MPVX vaccine, we aimed to explore optimal vaccine allocation between two linked GBMSM transmission networks over a short-term time horizon, across several epidemic conditions.

Methods. We constructed a deterministic compartmental MPVX transmission model. We parameterized the model to reflect two representative, partially connected GBMSM sexual networks (cities), using 2022 data from Ontario. We simulated a roll-out of 5000 vaccine doses over 30 days that started 45 days after epidemic seeding with 10 imported cases. Within this model, we varied: the relative city (network) sizes, epidemic potentials (R_0), between-city mixing, and distribution of seed cases between cities. For each combination of varied factors, we identified the allocation of doses between cities that maximized infections averted by day 90.

Results. Under our modelling assumptions, we found that a limited MPVX vaccine supply could generally avert more early infections when prioritized to: networks that were larger, had more initial infections, or had greater R_0. Greater between-city mixing decreased the influence of initial seed cases and increased the influence of city R_0 on optimal allocation. Under mixed conditions (e.g., fewer seed cases but greater R_0), optimal allocation required doses shared between cities.

Interpretation. In the context of the current global MPVX outbreak, we showed that prioritization of a limited supply of vaccines based on network-level factors can help maximize infections averted during an emerging epidemic. Such prioritization should be grounded in an understanding of context-specific risk drivers, and should acknowledge potential connectedness of multiple transmission networks.

1 Introduction

The emerging outbreak of monkeypox virus (MPVX) worldwide includes 1,435 cases in Canada as of 2022 October 287 [1]. A third-generation replication-deficient smallpox vaccine (Imvamune®) has been licensed for use against monkeypox and related orthopoxviruses in Canada since 2020, for the purpose of national security [2]. Shortly after cases were reported in Canadian cities, rapid pre-exposure prophylaxis vaccination efforts were started to help reduce acquisition, infectivity, and disease severity among communities disproportionately affected by MPVX, including gay, bisexual, and other men who have sex with men (GBMSM) [3,4]. However, jurisdictions across Canada and beyond were faced with a limited local supply of vaccines during the first few weeks of the MPVX outbreak.

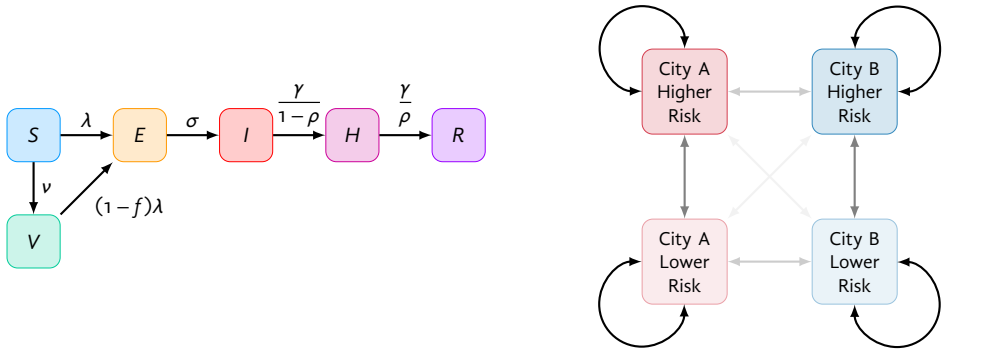
It is well-established that prioritizing a limited supply of vaccines to subpopulations with a disproportionately higher transmission risk (i.e., acquisition and/or transmission at the individual level and/or network levels) can maximize infections averted [5–8]. Such networks may have different characteristics that shape the epidemic potential within the network itself [9]. This potential is often quantified via the basic reproduction number R_0, which reflects the expected number of secondary infections generated by a person who is infected in a fully susceptible population [10]. A network's connectedness to other networks further shapes if and how many cases are imported by the time vaccine allocation decisions and roll-out begin [11].

We sought to explore optimal allocation of a fixed supply of MPVX vaccine across two partially connected transmission networks (reflecting jurisdictions) of GBMSM (reflecting the community with the most cases of MPVX infection currently) under different epidemic conditions. Specifically, we explored differences between two jurisdictions in: GBMSM population size; epidemic potential (R_0); imported/seed cases; and connectedness of the two jurisdictions. Our goal was to produce fundamental and generalizable insights into the prioritization of MPVX vaccine in the context of interconnected sexual networks, using jurisdictions (cities) within Ontario as an example, to guide policy-makers in allocating scarce vaccines to maximize infections averted.

2 Methods

2.1 Study Design

We constructed a deterministic compartmental model of MPVX transmission. Although stochastic network-based models can capture uncertainty and complex contact patterns better, deterministic compartmental models can estimate expected epidemic dynamics and have smaller data requirements, which are attractive during an emerging epidemic [12]. Risk heterogeneity and associated mixing patterns can also be captured in compartmental models via risk-based population stratification [13].



(a) Health states and transitions

(b) Cities, risk groups, and contact networks

Figure 1: Model structure

(b) High/Low R: risk groups; arrow opacity is proportional to contact network connectivity between groups. (a) *S*: susceptible; *V*: vaccinated; *E*: exposed; *I*: infectious; *R*: recovered. See Table A.1 and Appendix A for rate definitions.

2.2 Setting & Population

The modelled population represents 2 partially connected sexual transmission networks of GBMSM, although the model captures both sexual and nonsexual transmission. For the purposes of this study, we interpreted the two networks as two cities (cities A, B), having a combined GBMSM community size of 100,000 people.

To ground our analyses in a plausible epidemic context in Canada, we used the early MPVX situation in Ontario. The first reported case in Ontario occurred 2023 May 20 [14]; therefore, we posited possible exposures up to 21 days before in Toronto. Pre-exposure prophylaxis vaccination began 2022 June 12 [15]. At the time of initial vaccination rollout, about 5000 doses were available in Ontario and decisions were underway about optimal allocation of this limited supply across health units and cities in the province [16].

2.3 Model structure & Parameterization

Our model included 6 health states: susceptible, vaccinated, exposed, infectious, isolating, and recovered (Figure 1a). Each city was further stratified by levels of sexual risk (higher or lower, defined by the numbers of sexual partners) to reflect vaccine prioritization [2] and observed differences in the risk of MPVX infectionc [17] (Figure 1b). The definitions of higher and lower levels of sexual risk are outlined in Appendix A.

To parameterize the model, we drew on previous analyses of GBMSM sexual networks in Canada [18,19], and emerging MPVX epidemiological data in the context of the current epidemic [20–24]. We calibrated the average numbers of sexal partners among the higher-risk group to obtain city-specific R_0 that ranged from 1 to 2. Appendix A provides additional details about the model implementation and parameterization.

Table 1: Model parameters, including default values and ranges explored via grid sweep

Parameter	Stratum	Value	Range	Ref
Population size	overall	100,000		[18][a]
	fraction in city A	.50	[.20, .80]	[a]
Fraction higher risk	city A	.10	[.01, .50][b]	[18][a]
	city B	.10		[18][a]
Contact rate	close non-sexual, all	1		[25][a]
	sexual, lower risk	.01		[18][a]
	sexual, higher risk, city A	.189[c]	[.10, .25][b]	[18,26][a]
	sexual, higher risk, city B	.189[c]		[18,26][a]
Assortativity[d]	cities, all contacts	.90	[.70, 1.0]	[19][a]
	risk, close non-sexual	0		[a]
	risk, sexual	.50		[a]
Per-contact SAR	close non-sexual	.01[e]		[22,27]
	sexual	.90[c]		[26][a]
Initial infections	overall	10		[a]
	fraction in city A	.50	[0.0, 1.0]	[a]
Duration of period	latent/incubation	8		[22–24,28]
	infectious/symptoms	21		[21,22]
Fraction of infectious period isolated		.50		[22,29][a]
Vaccines available		5000		[a]
Vaccine effectiveness[f]		.85		[2,30,31]
Vaccine prioritization sensitivity	higher risk	.90		[3][a]
Vaccine allocation	city A	.50	[0.0, 1.0][g]	—

All durations in days; all rates in per-day. SAR: secondary attack rate. [a] Assumed / representative. [b] Calculated to fit $R_0 \in [1, 2]$. [c] Calculated to fit $R_0 = 1.5$, reflecting pre-vaccination estimate of MPVX R_0 in Ontario [14] via [10]. [d] Fraction of all contacts formed exclusively within-group; 0 implies random mixing; 1 implies no mixing. [e] Calibrated to fit approximately 95% incidence via sexual vs close, non-sexual contacts. [f] Leaky-type: partial protection among vaccinated. [g] Optimized parameter.

We initialized all simulations with 10 imported/seed cases in the higher-risk groups, distributed across the 2 cities as described in the Analysis subsection, and across the exposed, infectious, and isolating stages proportionally by mean stage duration.

2.4 Analysis

We simulated the distribution of 5000 vaccine doses over 30 days, starting 45 days after initial cases were imported (though not necessarily detected). Doses were imperfectly prioritized to the higher-risk group with 90% sensitivity (i.e., 4500 doses reach the higher risk group and 500 each the low risk group), reflecting early risk-based eligibility criteria in some jurisdictions [3].

With this fixed timeline and risk-based prioritization, we explored optimal vaccine allocation between cities A and B over a range of epidemic conditions. For a given set of conditions, we

defined the optimal vaccine allocation as that which resulted in the fewest cumulative infections by day 90 in both cities. We identified optimal allocation using the *optimize*[1] function in R.

We chose this 45-day time horizon and fixed 5000 vaccine doses to reflect a plausible medium-term optimization problem relevant to the early MPVX situation in Ontario. In reality, multiple changing time horizons may require consideration, different numbers of doses may become available, and different rates of vaccination may be possible. We aimed to obtain generalizable insights about the relationships between specific epidemic conditions and efficient geographic prioritization of a limited supply of vaccines during an outbreak.

As an example of one setting we analyzed, we chose parameters representative of a Toronto-like city (A) and another medium-sized Ontario city (B), with GBMSM population sizes of 80,000 and 20,000, respectively, and 10% sexual/social network connectivity ($\epsilon_c = 0.9$) [19]. We also modelled $R_0 = 2.0$ in city A versus 1.5 in city B, which reflects differences in sexual networks as suggested by differential prevalence of bacterial sexually transmitted infections across Ontario cities [32,33]. We simulated 100% imported/seed cases in city A, which reflects observed early MPVX case distribution in Ontario [14]. We then compared two strategies of vaccine allocation by city: proportional to population size; and "optimal" (fewest infections by day 9).

Next, we performed an uncertainty analysis of the following epidemic conditions, and identified the optimal vaccine allocation between cities A and B for each combination of conditions:

- relative size of city A versus B (1/4 to 4 times)
- relative epidemic potential in city A (R_0 in city A from 1 to 2, versus fixed 1.5 in city B), adjusted via the sexual activity of the higher risk group in the city A
- between-city mixing (0 to 30% of all contacts formed randomly between cities)
- fraction of imported/seed cases in city A versus B (0–100%)

We calculated city-specific R_0 assuming no inter-city mixing.

3 Results

Figure 2 illustrates modelled MPVX incidence and cumulative infections in city A versus city B under different strategies for vaccine allocation. Because of the larger population size, greater epidemic potential (R_0), and having all imported/seed cases in city A in this scenario, allocating all 5000 vaccine doses to city A yielded the fewest infections (550; solid line) by day 90 (optimal strategy). Allocating vaccines proportionally to city size yielded 615 infections (broken line), whereas no vaccination yielded 1020 infections (dotted line) (Figure 2 I; corresponding incidence rates in Figure 2 J).

Allocating most/all doses to city A allowed incidence to rise exponentially in city B. However, this approach can still avert more infections overall over shorter time horizons, after which

[1] https://www.rdocumentation.org/link/optimize?package=stats

more doses may become available. Figure B.1 illustrates the opposite case (default model parameters in Table 1): two identical cities with equal seeding, where the optimal allocation is equal between cities.

Figure 3 illustrates optimal vaccine allocation between cities A and B across different epidemic conditions. Figures B.2–B.5 further illustrate the absolute and relative numbers of infections averted under optimal allocation versus no vaccination (B.2–B.3), and versus vaccine allocation proportional to city size (B.4–B.5), showing under what conditions optimal allocation is most important.

We found that the strongest determinants of optimal vaccine allocation were: relative epidemic potential (R_0), share of seed cases, and city size, although the size of the higher-risk group was proportional to city size under our modelling assumptions. Thus, if a larger city had a large R_0 and most of the seed cases, it was best to allocate most/all doses to that city in our analysis (solid red/blue corners in Figure 3).

For smaller cities with large R_0 and most of the seed cases, it was sometimes possible to vaccinate the entire higher risk group; in such instances, the remaining doses were best allocated to the higher risk group in the other city, yielding the plateaus (solid yellow triangles) in Figure 3: (A,D,G) upper right; (C,F,I) lower left. This plateau shows how priority populations can change if/after high levels of coverage are achieved in other populations.

When cities with most/all seed cases had smaller R_0, doses were shared between cities under the optimal allocation strategy (to varying degrees), which suggests that both risk-based (reflecting R_0) and proximity-based (reflecting initial cases) prioritization strategies worked together to minimize transmission. In such instances, the other city necessarily had few/no seed cases but larger R_0, to which the same findings apply. These conditions are represented by the yellow diagonal segments in all facets of Figure 3.

Increased levels of mixing between cities mainly acted to reduce the influence of initial seed cases, and increase the influence of R_0 on optimal allocation of vaccines to each city (shown by the stronger vertical gradients [contours are relatively more horizontal] in Figure 3 [A,B,C] with more inter-city mixing, versus stronger horizontal gradients [contours are relatively more vertical] in [G,H,I] with less inter-city mixing).

4 Interpretation

We sought to explore how different epidemic conditions could affect optimal allocation of a fixed supply of MPVX vaccine across two partially connected transmission networks (e.g., cities or jurisdictions). Under our modelling assumptions, we found that: vaccines could generally avert more infections when prioritized to a larger network, a network with more initial infections, and a network with greater epidemic potential (R_0).

Although our study, for simplicity, focused on two partially-connected networks, it highlights the importance of measuring outcomes for a population overall, by considering that geographies are comprised of interconnected networks. That is, while cities across Canada, and globally, feature important within- and between-city differences in size and configuration of transmission networks [34,35], and in access to interventions and services [33,36,37], these cities ultimately remain connected with respect to transmission, and cannot be considered in iso-

lation over longer time horizons [19,35,38]. We grounded the 2 networks as "cities," but the implications would hold across geographic scope via vaccine allocation across health units, provinces, or even countries.

Within such interconnected settings, our findings are consistent with previous studies that showed that prioritizing limited vaccine supply/resources to communities or settings with the highest epidemic potential (shaped by density and other features of the contact network) generally yields the greatest benefit for the population overall [5,6,39]. We also identified how key factors, such as number of imported cases and connections between networks, shape efficient early vaccine roll-out.

Although our model parameterization reflected GBMSM sexual networks in Ontario, our findings have wider implications for vaccine roll-out globally. The persistent absence of vaccine supply and roll-out in regions already endemic for MPVX outbreaks across West and Central Africa, including (although not yet reported) in the context of GBMSM and sexual minorities [40], reflects another failure to uphold principles of equity in global health, paralleling missed opportunities in achieving COVID-19 vaccine equity [41]; such failures also undermine efforts to control and mitigate MPVX globally [42].

Prioritizing based on risk also requires understanding risk. Early vaccine roll-out in Ontario started in Toronto, where cases were already detected, the population size was large, and rates of bacterial sexually transmitted infections suggested a potentially denser sexual network and thus, greater epidemic potential [26]. Our model implemented differential R_0 between cities via contact rates; however, epidemic potential may also be linked to intervention access, including access to diagnoses and isolation support [36,43]. Thus, our findings suggest that characterizing the drivers of epidemic potential across jurisdictions and communities is important, including participatory, community-based surveillance and research into the contexts that lead to disproportionate risks at a network-level, not just at an individual-level [44,45].

4.1 Limitations

Our study aimed to provide fundamental and generalizable findings using a broad sensitivity analysis to identify conditions that can shape optimal short-term vaccine allocation with a limited supply. As with any modelling study, our results depended on our modelling assumptions and parameter values; for some of these, limited data were available. We did not evaluate population-level benefits balanced with potential adverse effects, given existing data on high safety with the smallpox vaccines used in Canada [46,47].

We used a simple compartmental model, with only two risk groups; future work would benefit from more nuanced representations of risk (e.g., using individual-based sexual network models). Our study also explored only two representative GBMSM transmission networks (cities) with a fixed number of doses. Incorporation of the wider population, additional transmission networks, or calibration to observed data on cases, service availability, and vaccine uptake in specific cities or relevant jurisdictions, could yield more interesting prioritization findings. However, we expect that our findings using thest two networks would apply across multiple networks and conditions.

Finally, we restricted our study to a limited vaccine supply with a fixed rollout approach, and future research would benefit from exploring the sensitivity of results to different amounts of finite supply, time–variant vaccination rate, and number of imported/seed cases, as well as timing of vaccine availability in relation to epidemic phase.

5 Conclusion

Strategic prioritization of a limited vaccine supply by network-level risk factors can maximize infections averted over short time horizons in the context of an emerging epidemic, such as the current global MPVX outbreak. Notable factors include: the network size, distribution of initial cases, relative epidemic potential within a given network, and connectivity between networks. Such epidemic potential is defined not just by possible modes of transmission but by network configuration, access to prevention and care, and by underlying social and structural contexts. Efforts to understand and anticipate epidemic potential across and between different networks before outbreaks occur can support rapid response. Such efforts should be paired with resource prioritization to eliminate existing disparities in health care access and outcomes.

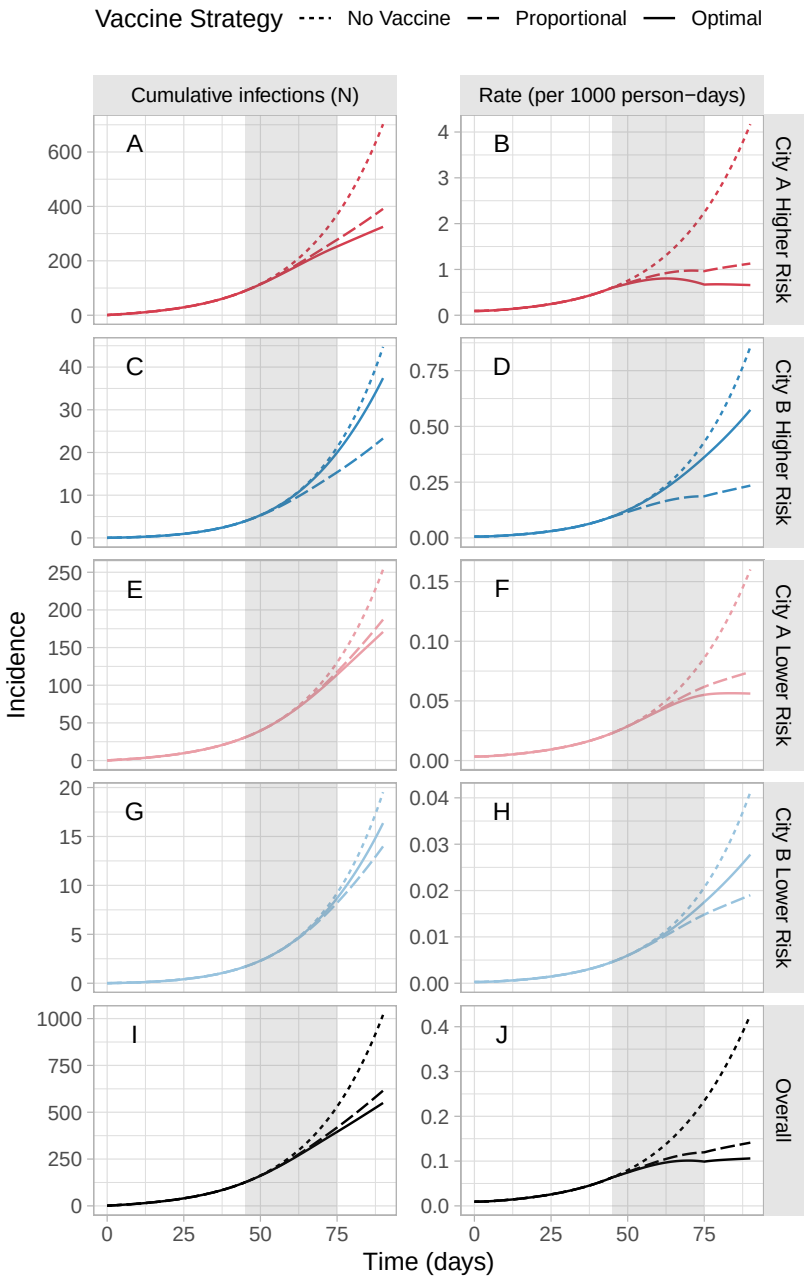


Figure 2: Modelled MPVX cumulative infections and incidence in two cities under three different vaccine allocation scenarios

Gray bar indicates period of vaccine roll-out (days 45–75). City A reflects a Toronto-like city and city B reflects a medium-sized city in Ontario. For vaccine allocation, proportional allocation (to city size) was 75% to city A and 25% to city B; while optimal allocation (most infections averted by day 90) was 100% to city A. Risk: risk of MPVX infection or transmission, defined by numbers of sexual partners (definitions in Appendix A.)

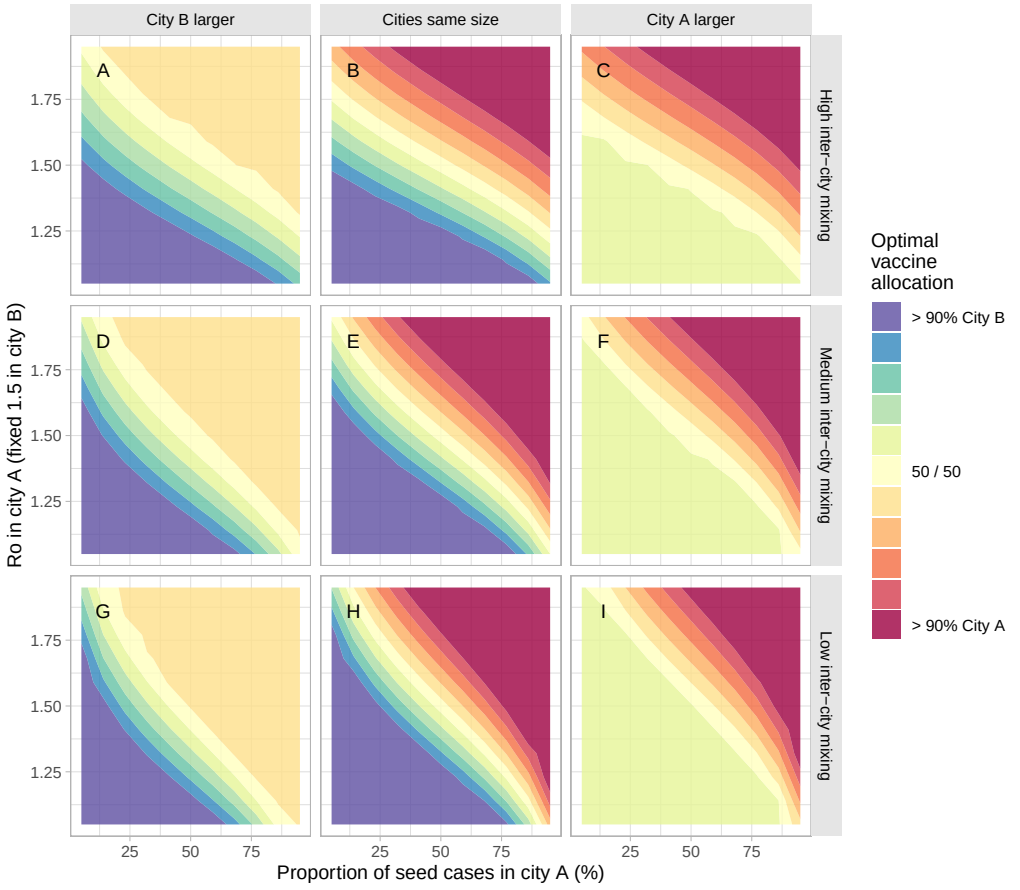


Figure 3: Optimal MPVX vaccine allocation between two cities under different epidemic conditions

Epidemic potential (R_0) in city A varies via the sexual activity among the high risk group in city A. We definedd optimal allocation as fewest cumulative infections by day 90. The larger city is 3 times the size of the other city. We used city assortativity ϵ_c values of 0.80, 0.90, and 0.95 for high, moderate, and low between-city mixing, respectively.

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Contributions

JK and SM conceptualized and designed the study, and drafted the manuscript. JK developed the model, conducted the analyses and generated the results. SM and DT provided key interpretation of the results. DT contributed critical review of the manuscript. All authors contributed to addressing revisions, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

Data Availability

All analysis code is available at `github.com/mishra-lab/mpox-model-compartmental`. Figures and numeric results can be obtained directly from this code using R.

APPENDIX

Title: Maximizing the impact of limited vaccine supply under different early epidemic conditions: a 2-city modelling analysis of monkeypox virus transmission among men who have sex with men

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Date: 2022 Nov 28

A Model Details

Table A.1 summarizes the notation used, and Figure 1 illustrates the model structure, repeated (verbatim) in Figure A.1 for easier reference.

Table A.1: Notation

Symbol	Definition
c	city index $\in$ {A, B}
r	risk group index $\in$ {high, low}
y	type of contact index $\in$ {sexual, close non-sexual}
x'	index "x" for a contact, versus self
N	population size
C	contact rate
Q	total contacts offered: NC
ϵ	assortativity parameter $\in$ [1: assortative, 0: random]
λ	incidence rate (force of infection)
β	secondary attack rate [a]
σ^{-1}	duration of latent/incubation period
γ^{-1}	duration of infectious/symptom period
Φ	probability of contact formation
ρ	proportion isolating among infectious
ν	vaccination rate
f	vaccine effectiveness (leaky-type)

All durations in days; all rates in per-day. [a] per-partnership transmission probability.

A.1 Differential Equations

Equation (A.1) summarizes the system of differential equations for the health states; each equation is repeated for each combination of city c (A, B) and risk group r (higher, lower) (4 total), but we omit the cr index notation for clarity.

$$\frac{d}{dt}S = -\nu S - \lambda S \tag{A.1a}$$

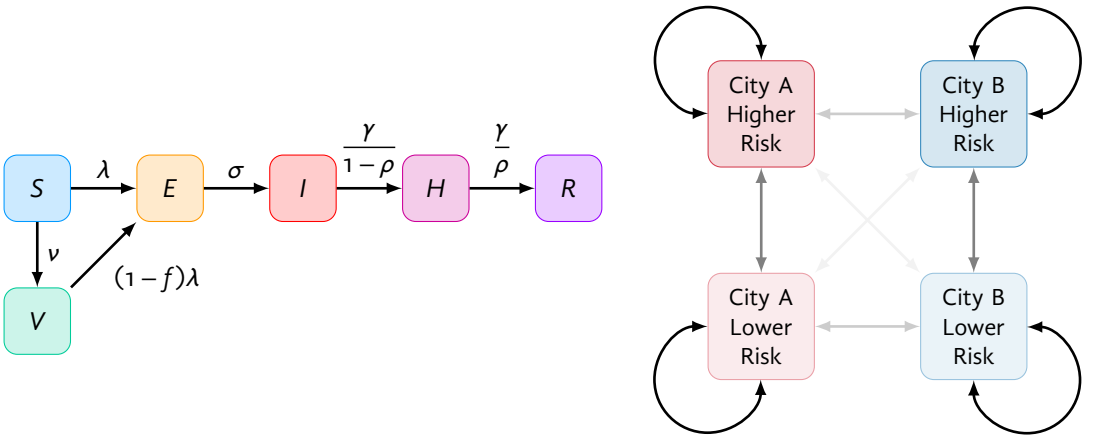
$$\frac{d}{dt}V = +\nu S - (1-f)\lambda V \tag{A.1b}$$

$$\frac{d}{dt}E = +\lambda S + (1-f)\lambda V - \sigma E \tag{A.1c}$$

$$\frac{d}{dt}I = +\sigma E - \frac{\gamma}{1-\rho}I \tag{A.1d}$$

$$\frac{d}{dt}H = +\frac{\gamma}{1-\rho}I - \frac{\gamma}{\rho}H \tag{A.1e}$$

$$\frac{d}{dt}R = +\frac{\gamma}{\rho}H \tag{A.1f}$$



(a) Health states and transitions

(b) Cities, risk groups, and contact networks

Figure A.1: Model structure

(a) S: susceptible; V: vaccinated; E: exposed; I: infectious; H: isolating; R: recovered. (b) Arrow opacity is qualitatively related to the chance of sexual contact formation from any group to another. See Table A.1 for rate definitions.

A.2 Incidence Rate

The incidence rate (force of infection) for non-vaccinated susceptible individuals in city c and risk group r ("group cr") is defined as:[2]

$$\lambda_{cr} = \sum_{yc'r'} \beta_y \, C_{ycr} \, \Phi_{ycrc'r'} \, \frac{I_{c'r'}}{N_{c'r'}} \tag{A.2}$$

where: β_y is the transmission probability per type-y contact; C_{ycr} is the type-y contact rate among group cr; $\Phi_{ycrc'r'}$ is the probability of forming a type-y contact with group $c'r'$ (contacts) among group cr (self); and N_{cr} is the size of group cr.

Among vaccinated, the incidence rate is simply reduced by a factor $(1 - f)$, where f is the vaccine effectiveness (leaky-type).

A.3 Mixing

Mixing between risk groups and cities was implemented using an adaptation of a common approach [1,2]. We denote the total contacts "offered" by group cr as: $Q_{cr} = N_{cr}C_{cr}$; and denote the margins (sums) $Q_c = \sum_r Q_{cr}$; $Q_r = \sum_c Q_{cr}$; and $Q = \sum_{cr} Q_{cr}$. The probability of

[2] The online Appendix to the published paper erroneously includes a term "$(1 - \rho)$" in (A.2), which should have been removed after the isolating state H was added during revisions.

contact formation with group $c'r'$ among group cr is defined as:

$$\Phi_{crc'r'} = \epsilon_c \delta_{cc'} \left(\epsilon_r \delta_{rr'} + (1 - \epsilon_r) \frac{Q_{c'r'}}{Q_{c'}} \right) + (1 - \epsilon_c) \frac{Q_{c'}}{Q} \left(\epsilon_r \delta_{rr'} + (1 - \epsilon_r) \frac{Q_{r'}}{Q} \right) \tag{A.3}$$

where: $\delta_{ii'} = \{1 \text{ if } i = i'; 0 \text{ if } i \neq i'\}$ is an identity matrix; and $\epsilon_c, \epsilon_r \in [0, 1]$ are assortativity parameters for mixing among cities and risk groups, respectively, such that $\epsilon = 1$ yields complete group separation and $\epsilon = 0$ yields completely random (proportionate) mixing. For clarity, we omit the index of contact type y, although ϵ_r, C_{cr} and thus $\Phi_{crc'r'}$ are all further stratified by y.

A.4 City R_0

The basic reproduction number R_0 for each city was defined in the absence of vaccination and ignoring between-city mixing — i.e., with $\epsilon_c = 1$. Following [3], we define R_0 as the dominant eigenvalue of the city-specific next generation matrix K; matrix elements $K_{rr'}$ are defined as:

$$K_{rr'} = (1 - \rho) \sum_y \beta_y C_{yr} \Phi_{yrr'} \frac{N_r}{N_{r'}} \gamma^{-1} \tag{A.4}$$

where: ρ is the proportion isolating among infectious; β_y is the transmission probability per type-y contact; C_{yr} is the type-y contact rate among group r; $\Phi_{yrr'}$ is the probability of type-y contact formation with group r' among group r; N_r is the size of group r; and γ^{-1} is the duration of infectiousness.

A.5 Vaccine Allocation

Vaccination is modelled as distribution of 5000 doses over 30 days from day 45 (167 doses per day). Vaccines are prioritized to the high risk group with 90% sensitivity, such that 4500 doses actually reach the high risk group, and 500 doses are given to the lower risk group. Figure A.2 illustrates vaccination coverage/counts by city/risk group for an example allocation of 80% to city A and 20% to city B.

A.6 Parameterization

Model parameter values and stratifications are summarized in Table 1, repeated (verbatim) in Table A.2 for easier reference.

Risk Groups and Sexual Contacts: Parameterization of risk groups and contacts was primarily informed by existing analyses conducted to support mathematical modelling of HIV-transmission among GBMSM in Canada [4, n.b. Appendix 3.2], since sexual history data among GBMSM diagnosed with MPVX in Canada are not yet available. These analyses stratified GBMSM into 88–94% lower risk, with on average 4 sexual partners per-year ($\approx$ .01 per day), and 6–12% higher risk, with approximately 6-times as many partners ($\approx$ .07 per day), reflecting common stratification corresponding to rates of bacterial STI and partner number distributions [21,22]. Our present model includes even greater partner numbers among the higher

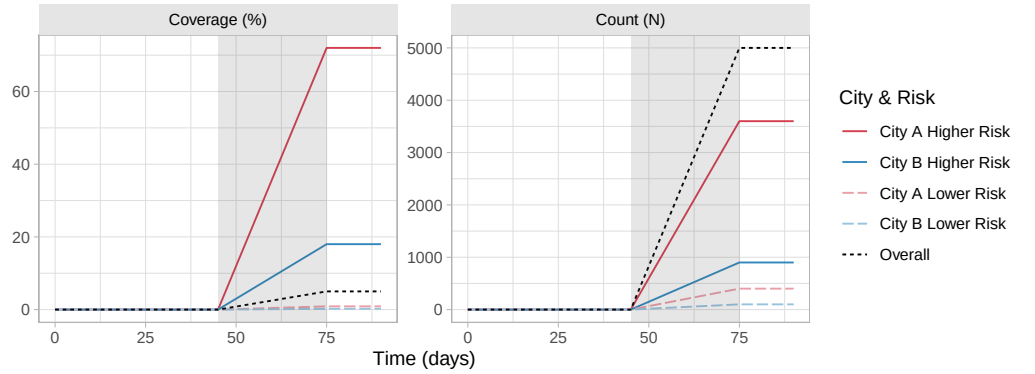


Figure A.2: Example vaccine allocation: 80% to city A, and 90% to high risk group

Gray bar indicates period of vaccine roll-out (days 45–75)

risk group (.10–.25 per day), partly to fit MPVX $R_0 \in [1, 2]$, and because the 6-fold value in [4] was mainly applied as a generalized proxy for 6-times higher HIV incidence. Weighted pooling of data from three studies [23–25] suggested that approximately 12% of respondents reported 20+ sexual partners in the past 6 months ($\approx$ .11+ per day). Our MPVX model also models transmission risk per-partnership, versus per-contact (sex act) as in [4]; with high SAR, MPVX transmission risk would be expected to be driven more by numbers of partners than by total contacts (sex acts).

A retrospective and rapid sexual history survey of 45 individuals diagnosed with MPVX identified that 60% (27 of 45) were diagnosed with an STI in the previous year, 44% (20 of 45) reported more than 10 sexual partners in the previous 3 months, and 44% (20 of 45) reported group sex during the incubation period [26].

Close, Non-Sexual Contacts: We defined close, non-sexual contacts as direct exposure of broken skin or mucous membranes, or to bodily fluids or potentially infectious material (including clothing or bedding) without appropriate personal protective equipment, such as sleeping in the same bed. Based on available data on types of partnerships, 30–60% of GBMSM in Canada report a regular sex partner [5], and data on additional living conditions (such as cohabitating with non-sexual partners) was not available.

Network Connectivity: There is limited data on proportion of contacts (sexual and close non-sexual) formed between different regional GBMSM networks, Such proportions will also depend on the geographic scale of the networks considered, while our study aimed to be generalizable across scales. In [7] 37.5% of 269 respondents from Waterloo, Ontario had travelled outside the region for sex; however, this does not necessarily reflect the proportion of all sex outside the region. From limited case-series data, evidence suggests that a smaller fraction have likely acquired MPVX infection via sex in other cities: among cases among Toronto residents seen at Unity Health Toronto between 2022 May 20 and July 15: 2/27 were identified as infection from sexual exposures outside Toronto [27, personal communication].

Monkeypox Virus (MPVX) & Reproduction Number: Updated epidemiological data on MPVX infection and transmission in the context of the present epidemic are rapidly emerging [9,28].

Table A.2: Model parameters, including default values and ranges explored via grid sweep

Parameter	Stratum	Value	Range	Ref
Population size	overall	100,000		[4][a]
	fraction in city A	.50	[.20, .80]	[a]
Fraction higher risk	city A	.10	[.01, .50][b]	[4][a]
	city B	.10		[4][a]
Contact rate	close non-sexual, all	1		[5][a]
	sexual, lower risk	.01		[4][a]
	sexual, higher risk, city A	.189[c]	[.10, .25][b]	[4,6][a]
	sexual, higher risk, city B	.189[c]		[4,6][a]
Assortativity[d]	cities, all contacts	.90	[.70, 1.0]	[7][a]
	risk, close non-sexual	0		[a]
	risk, sexual	.50		[a]
Per-contact SAR	close non-sexual	.01[e]		[8,9]
	sexual	.90[c]		[6][a]
Initial infections	overall	10		[a]
	fraction in city A	.50	[0.0, 1.0]	[a]
Duration of period	latent/incubation	8		[9–12]
	infectious/symptoms	21		[9,13]
Fraction of infectious period isolated		.50		[9,14][a]
Vaccines available		5000		[a]
Vaccine effectiveness[f]		.85		[15–17]
Vaccine prioritization sensitivity	higher risk	.90		[18][a]
Vaccine allocation	city A	.50	[0.0, 1.0][g]	—

All durations in days; all rates in per-day. SAR: secondary attack rate. [a] Assumed / representative. [b] Calculated to fit $R_0 \in [1, 2]$. [c] Calculated to fit $R_0 = 1.5$, reflecting pre-vaccination estimate of MPVX R_0 in Ontario [19] via [20]. [d] Fraction of all contacts formed exclusively within-group; 0 implies random mixing; 1 implies no mixing. [e] Calibrated to fit approximately 95% incidence via sexual vs close, non-sexual contacts. [f] Leaky-type: partial protection among vaccinated. [g] Optimized parameter.

In the absence of high-quality evidence on the secondary attack rate (SAR) of sexual transmission, we assumed a relatively high SAR of 0.9 (per-partnership), drawing on local patient histories, and in order to reproduce $R_0 \in [1, 2]$. We estimated $R_0 \in [1, 2]$ using MPVX case data from Ontario [19] before widespread vaccine roll-out (2022 May 13 – July 4) using the `EpiNow2` R package [20]. We further calibrated the SAR for close, non-sexual to reproduce approximately 95% incidence via sexual vs close, non-sexual contacts [29].

In another model [6], the modelled R_0 for a GBMSM sexual network was greater, even for smaller SAR. Two main factors may explain this discrepancy in modelled R_0 vs SAR in [6] vs our model. First, isolation was not explicitly modelled in [6]; thus the reported SAR in [6] can be considered as after considering isolation, i.e., reduced. Second, the branching process model in [6] captured greater risk heterogeneity than our model, and focused especially on capturing the highest levels of risk ("heavy tail"). Such heterogeneity is directly related to R_0 through the coefficient of variation in contact rates [30]. Thus, this difference in model structure could further explain why modelled R_0 would be greater in [6], for even similar

SAR. Finally, our aim was to obtain generalizable insights about network-level vaccine prioritization, rather than to model specific contexts within Ontario; as such, we do not expect our main findings to change with moderate changes to the model simplifications regarding transmission.

B Supplemental Results

Figure B.1 illustrates incidence rate and cumulative infections (similar results to Figure 2), for two cities identical in: size, R_0, and imported/seed cases, under three vaccination scenarios: no vaccination, 100% allocation to city A, and equal allocation between cities. Equal allocation minimizes cumulative infections.

Figures B.2–B.5 illustrate cumulative infections averted by day 90 under "optimal" vaccine allocation: versus no vaccination (absolute: B.2, relative: B.3), and versus allocation proportional to city size (absolute: B.4, relative: B.5).

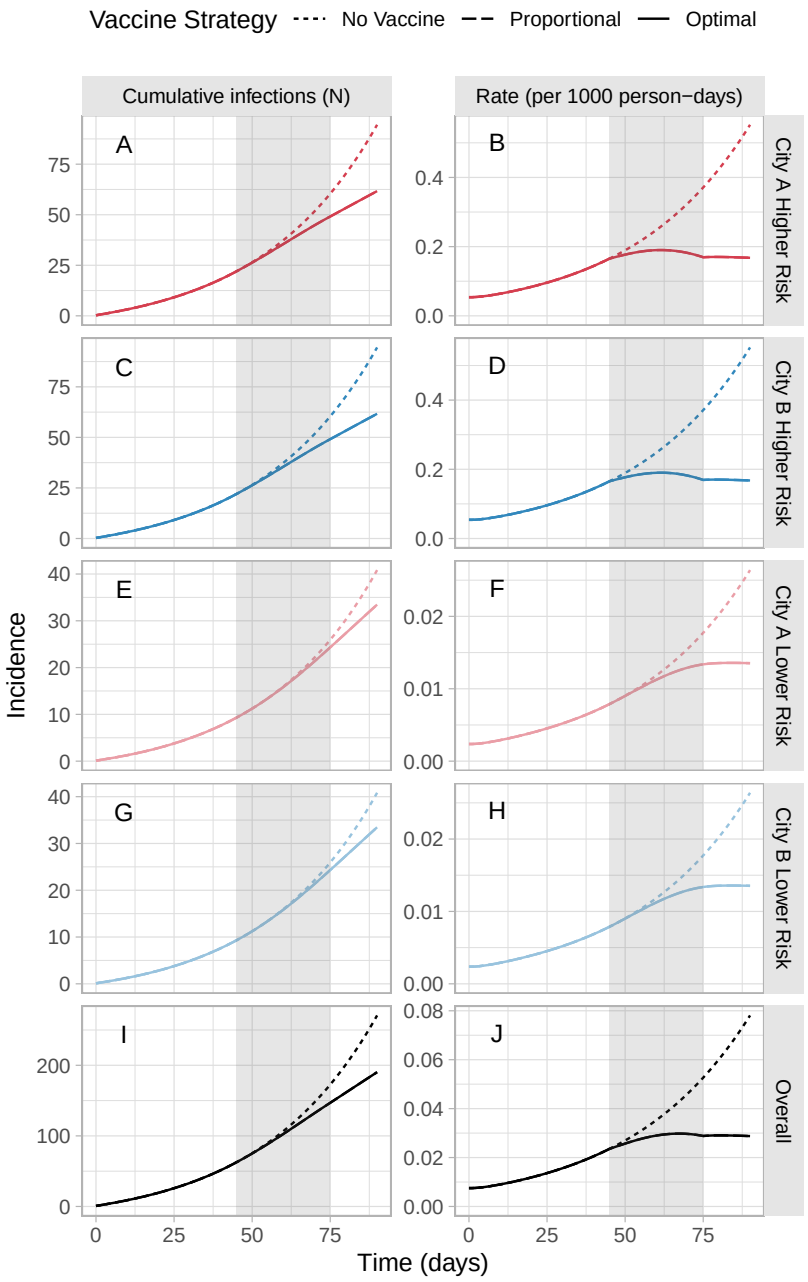


Figure B.1: Modelled MPVX incidence and cumulative infections in cities A and B with default parameters, under two different vaccine allocation scenarios

Gray bar indicates period of vaccine roll-out (days 45–75). Risk: risk of MPVX infection or transmission, defined by numbers of sexual partners. The proportional case is not visible because it overlaps exactly with the optimal case.

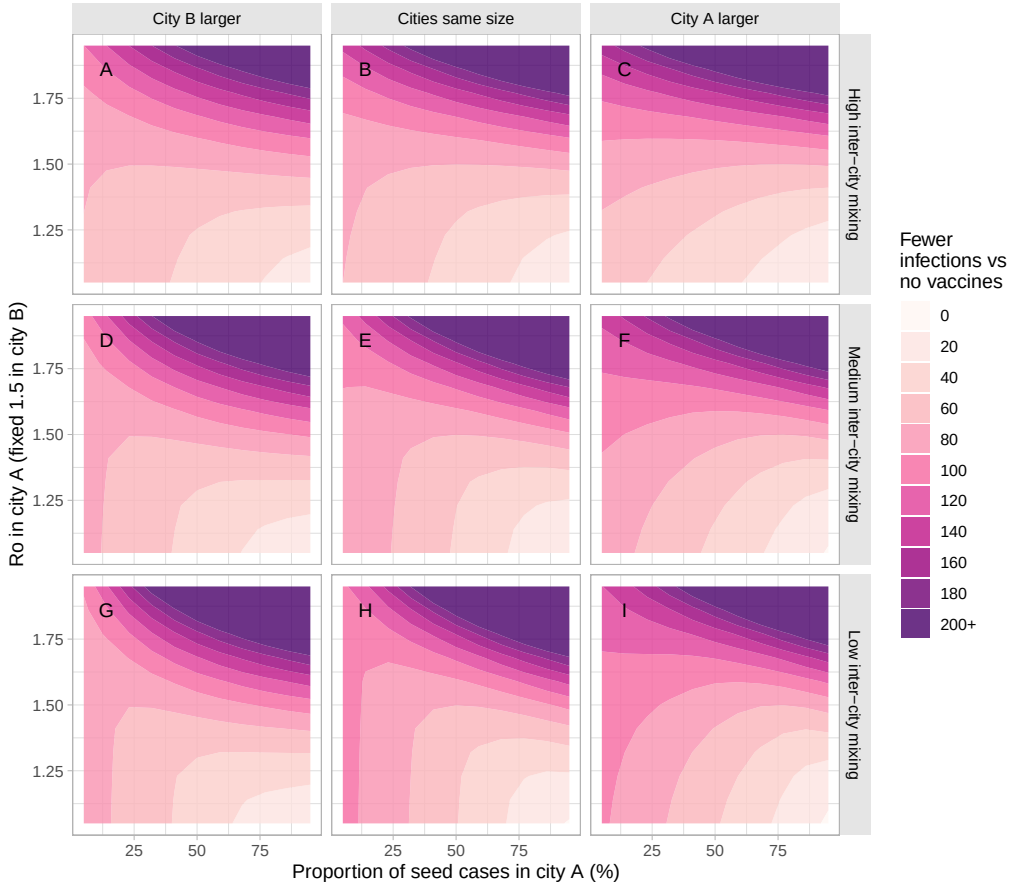


Figure B.2: Absolute fewer infections under optimal vaccine allocation versus no vaccination

Epidemic potential (R_0) in city A varies via the sexual activity among the high risk group in city A. We definedd optimal allocation as fewest cumulative infections by day 90. The larger city is 3 times the size of the other city. We used city assortativity ϵ_c values of 0.80, 0.90, and 0.95 for high, moderate, and low between-city mixing, respectively.

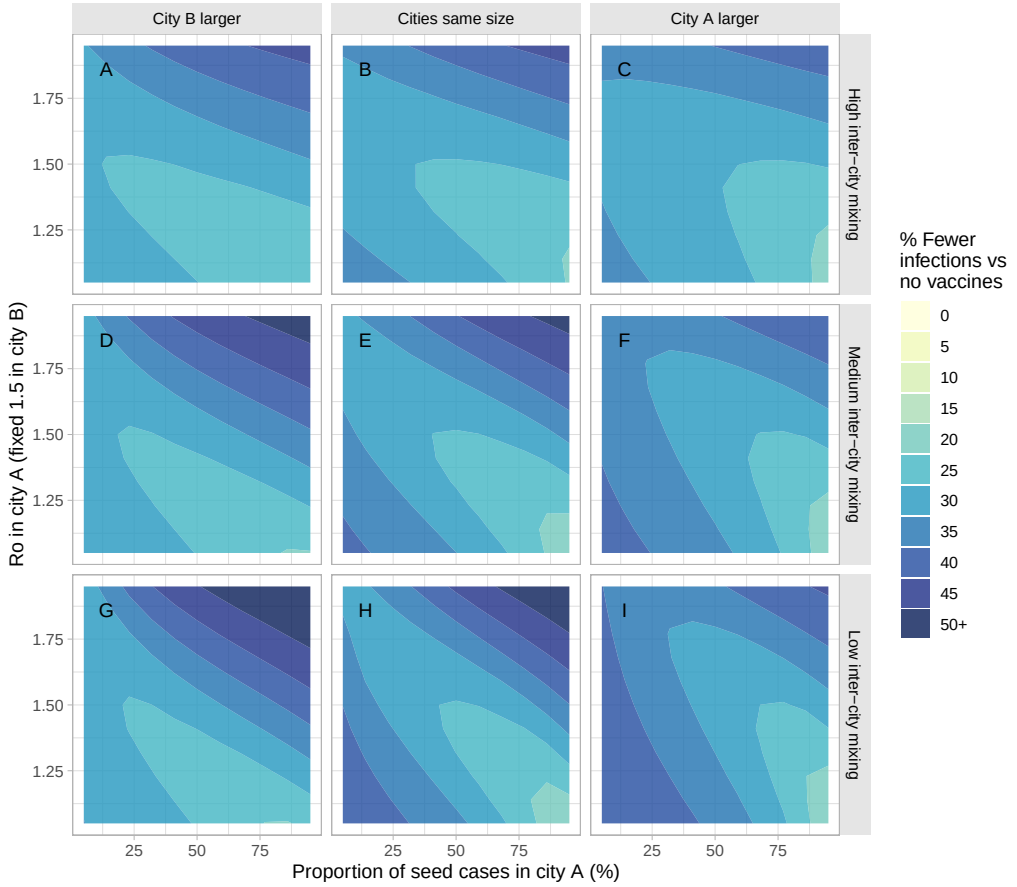


Figure B.3: Relative fewer infections under optimal vaccine allocation versus no vaccination

Epidemic potential (R_0) in city A varies via the sexual activity among the high risk group in city A. We definedd optimal allocation as fewest cumulative infections by day 90. The larger city is 3 times the size of the other city. We used city assortativity ϵ_c values of 0.80, 0.90, and 0.95 for high, moderate, and low between-city mixing, respectively.

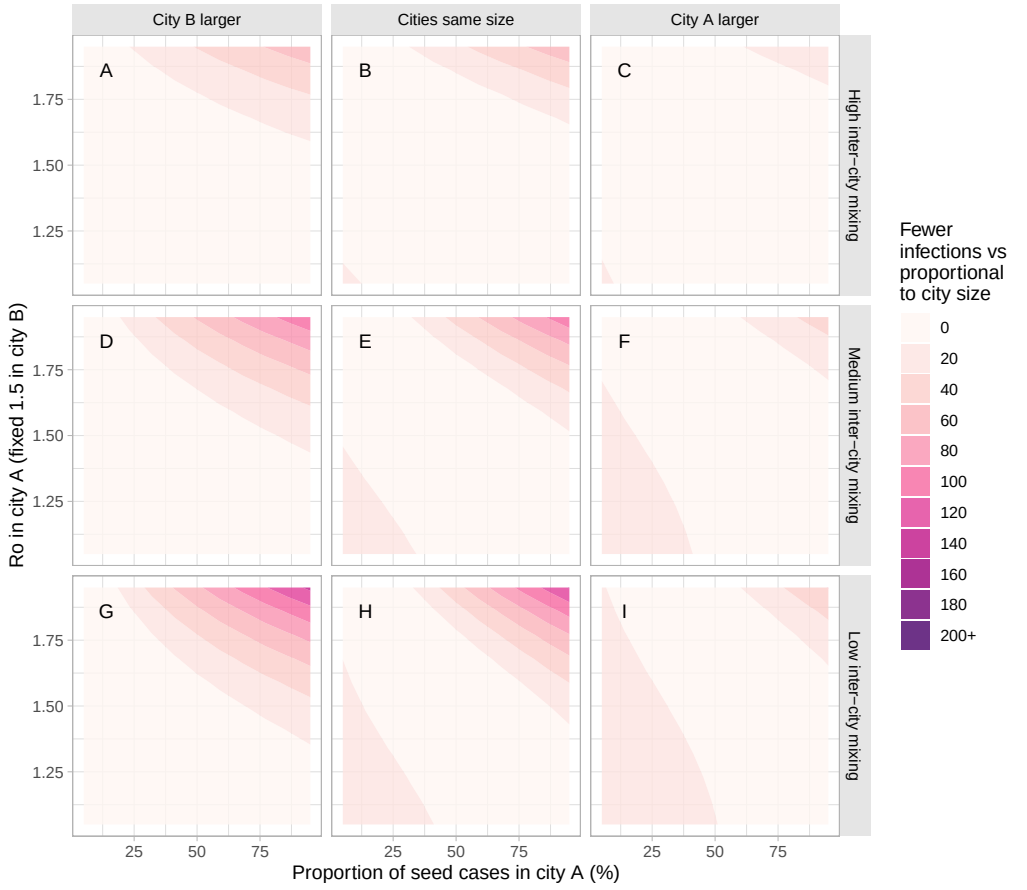


Figure B.4: Absolute fewer infections under optimal vaccine allocation versus allocation proportional to city size

Epidemic potential (R_0) in city A varies via the sexual activity among the high risk group in city A. We definedd optimal allocation as fewest cumulative infections by day 90. The larger city is 3 times the size of the other city. We used city assortativity ϵ_c values of 0.80, 0.90, and 0.95 for high, moderate, and low between-city mixing, respectively.

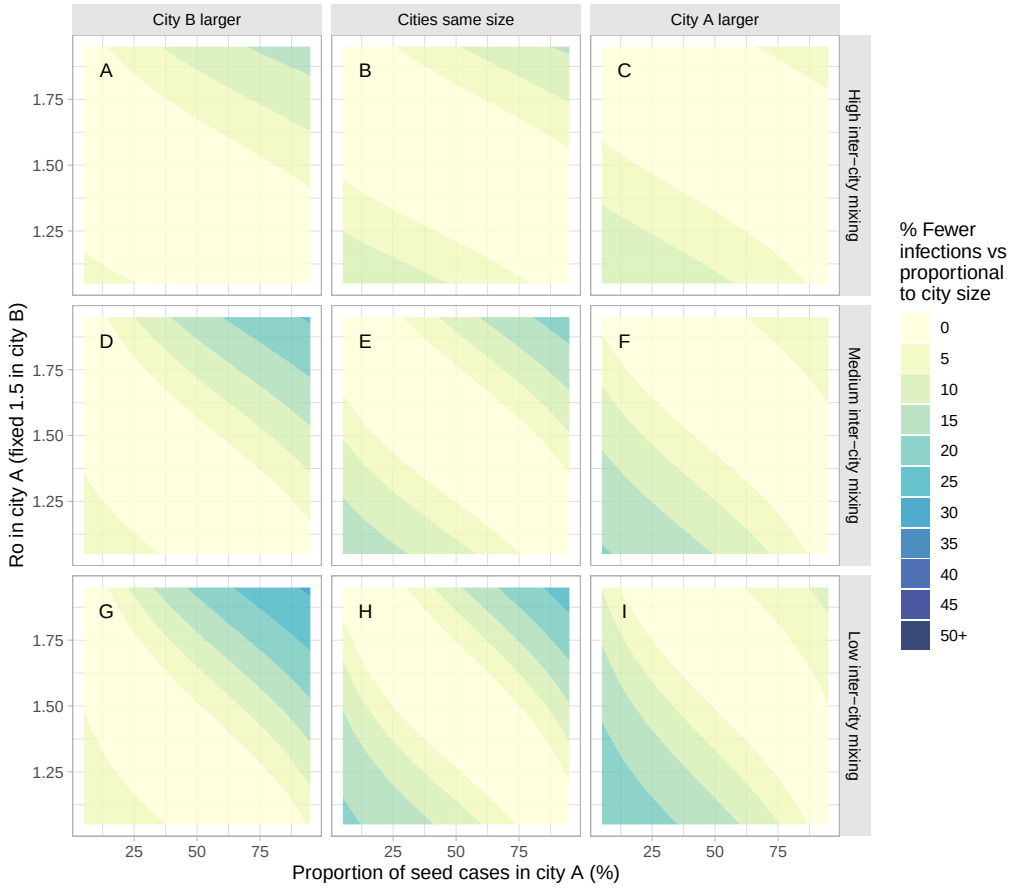


Figure B.5: Relative fewer infections under optimal vaccine allocation versus allocation proportional to city size

Epidemic potential (R_0) in city A varies via the sexual activity among the high risk group in city A. We definedd optimal allocation as fewest cumulative infections by day 90. The larger city is 3 times the size of the other city. We used city assortativity ϵ_c values of 0.80, 0.90, and 0.95 for high, moderate, and low between-city mixing, respectively.

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