Appendix 1

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

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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 act as guarantors of the work.

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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.

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A: Model Details

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

Table A1. Notation

Symbol	Definition [a]
c	city index ϵ {A, B}
r	risk group index ϵ {higher, lower}
y	type of contact index ϵ {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 ϵ [1: assortative, 0: random]
λ	incidence rate (force of infection)
β	secondary attack rate [b]
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)

[a] all durations in days; all rates in per-day. [b] 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.

$$\frac{d}{dt}S = -\nu S - \lambda S$$
$$\frac{d}{dt}S = +\nu S - (1-f)\lambda V$$
$$\frac{d}{dt}E = +\lambda S + (1-f)\lambda V - \sigma E$$
$$\frac{d}{dt}I = +\sigma E - \frac{\gamma}{1-\rho}I$$
$$\frac{d}{dt}H = +\frac{\gamma}{1-\rho}I - \frac{\gamma}{\rho}H$$
$$\frac{d}{dt}R = +\frac{\gamma}{\rho}H$$

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:

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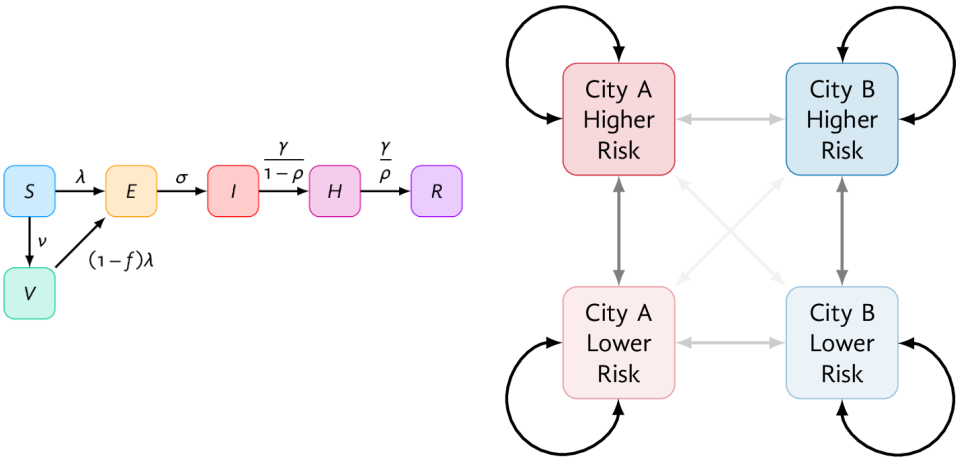

(a) Health states and transitions (b) Cities, risk groups and contact networks

Figure A.1. Model structure

(a) S: susceptible; V: vaccinated; E: exposed; I: infectious; H: isolating; R: recovered. (b) Risk: of MPXV infection/transmission, defined by numbers of sexual partners. Arrow opacity is qualitatively related to the chance of sexual contact formation from any group to another (higher opacity reflects greater chance of contact). See Appendix 1 Section A (model details) for rate definitions.

$$\lambda_{cr} = \sum_{yc'r'} (1-\rho)\ \beta_y\, C_{ycr}\, \Phi_{ycrc'r'} \frac{I_{c'r'}}{N_{c'r'}}$$

where: ρ is the proportion isolating among infectious; 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 contact formation with group $c'r'$ among group cr is defined as:

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

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.

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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:

$$K_{rr'} = (1 - \rho) \sum_{y} \beta_y C_{yr} \Phi_{yrr'} \frac{N_r}{N_{r'}} \gamma^{-1}$$

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.

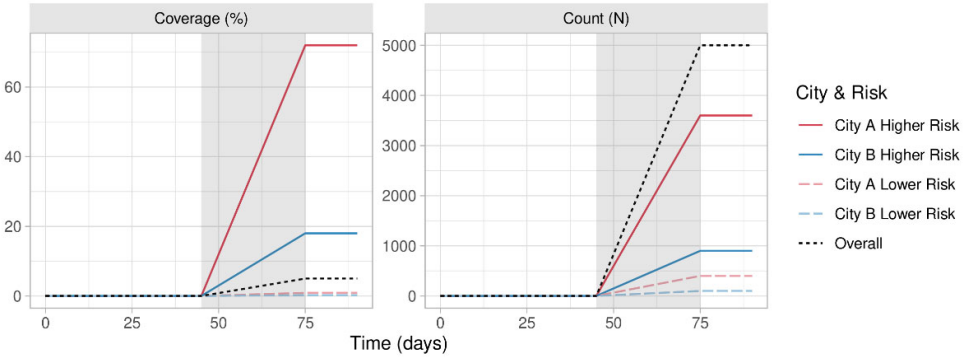

Figure A.2. Example vaccine allocation: 80% to city A, and 90% to high risk group

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

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, p. Appendix 3.2], since sexual history data among GBMSM diagnosed with MPXV in Canada are not yet available. These analyses stratified GBMSM into 88–94% lower risk, with on average 4 sexual partners per-year (≈ .01 per day), and 6–12% higher risk, with approximately 6-times as many partners (≈ .07 per day), reflecting common stratification corresponding to rates of bacterial STI and partner number distributions [21, 22].

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

Parameter [a]	Stratum	Value	Range	Ref
Population size	overall	100,000		[18] [b]
	fraction in city A	.50	[.20, .80]	[b]
Fraction higher risk	city A	.10	[.01, .50] [c]	[18] [b]
	city B	.10		[18] [b]
Contact rate	close non-sexual, all	1		[27] [b]
	sexual, lower risk	.01		[18] [b]
	sexual, higher risk, city A	.189 [d]	[.10, .25] [c]	[18, 28] [b]
	sexual, higher risk, city B	.189 [d]		[18, 28] [b]
Assortativity [e]	cities, all contacts	.90	[.70, 1.0]	[19] [b]
	risk, close non-sexual	0		[b]
	risk, sexual	.50		[b]
Per-contact SAR	close non-sexual	.01 [f]		[29, 22]
	sexual	.90 [d]		[28] [b]
Initial infections	overall	10		[b]
	fraction in city A	.50	[0.0, 1.0]	[b]
Duration of period	latent/incubation	8		[22, 24, 23, 30]
	infectious/symptoms	21		[21, 22]
Fraction of infectious period isolated	all	.50		[22, 31] [b]
Vaccines available	all	5000		[b]
Vaccine effectiveness [g]	all	.85		[21, 22, 23]
Vaccine prioritization sensitivity	higher risk	.90		[3] [b]
Vaccine allocation	city A	.50	[0.0, 1.0] [h]	–

Note: [a] All durations in days; all rates in per-day. SAR: secondary attack rate. [b] Assumed or representative. [c] Calculated to fit R_0 [1, 2]. [d] Calculated to fit R_0 = 1.5, reflecting pre-vaccination estimate of MPVX R_0 in Ontario [14] via [10]. [e] Fraction of contacts formed exclusively within-group [34]; 0 implies random mixing between groups and 1 implies no mixing. [f] Calibrated to fit approximately 95% incidence via sexual vs close, non-sexual contacts. [g] Leaky-type: partial protection among all vaccinated, not full protection among a fraction vaccinated. [h] Optimized parameter.

Our present model includes even greater partner numbers among the higher risk group (.10–.25 per day), partly to fit MPXV $R_0 \in [1, 2]$, 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, 24, 25] suggested that approximately 12% of respondents reported 20+ sexual partners in the past 6 months ($\approx .11+$ per day). Our MPXV model also models transmission risk per-partnership, versus per-contact (sex act) as in [4]; with high SAR, MPXV 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 MPXV 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

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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 MPXV 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].

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

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B: Supplemental Results

Figure B.1 illustrates incidence rate and cumulative infections (similar results to Figure 2), for 2 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).

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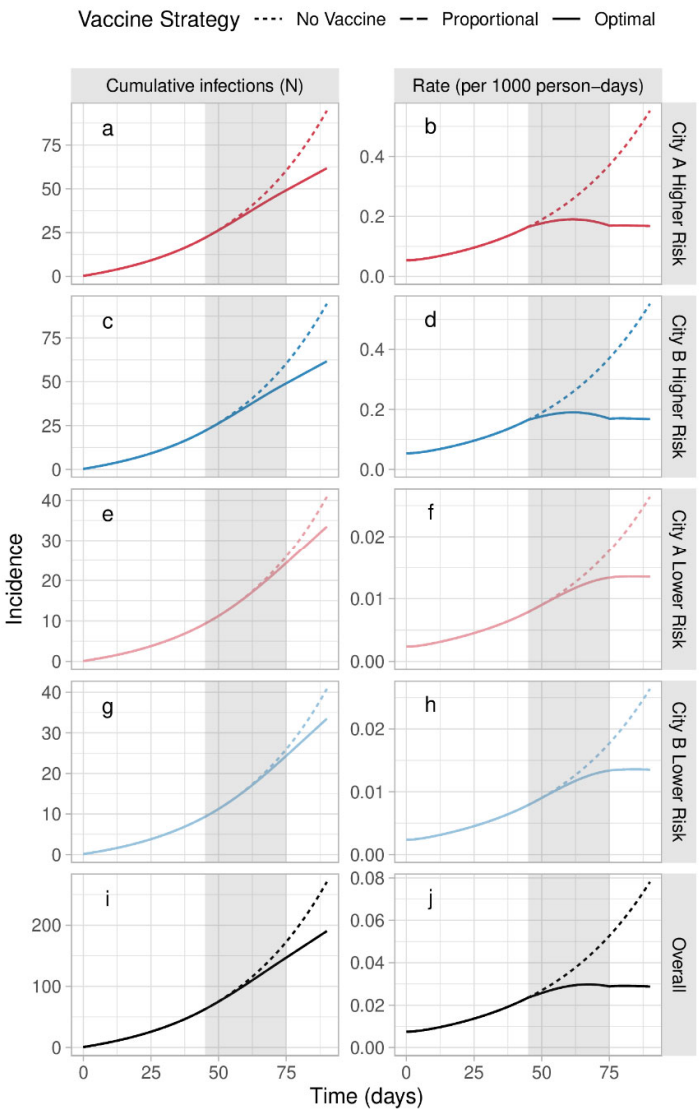

Figure B.1. Modelled monkeypox incidence and cumulative infections in cities A and B with default parameters, under 2 different vaccine allocation scenarios

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

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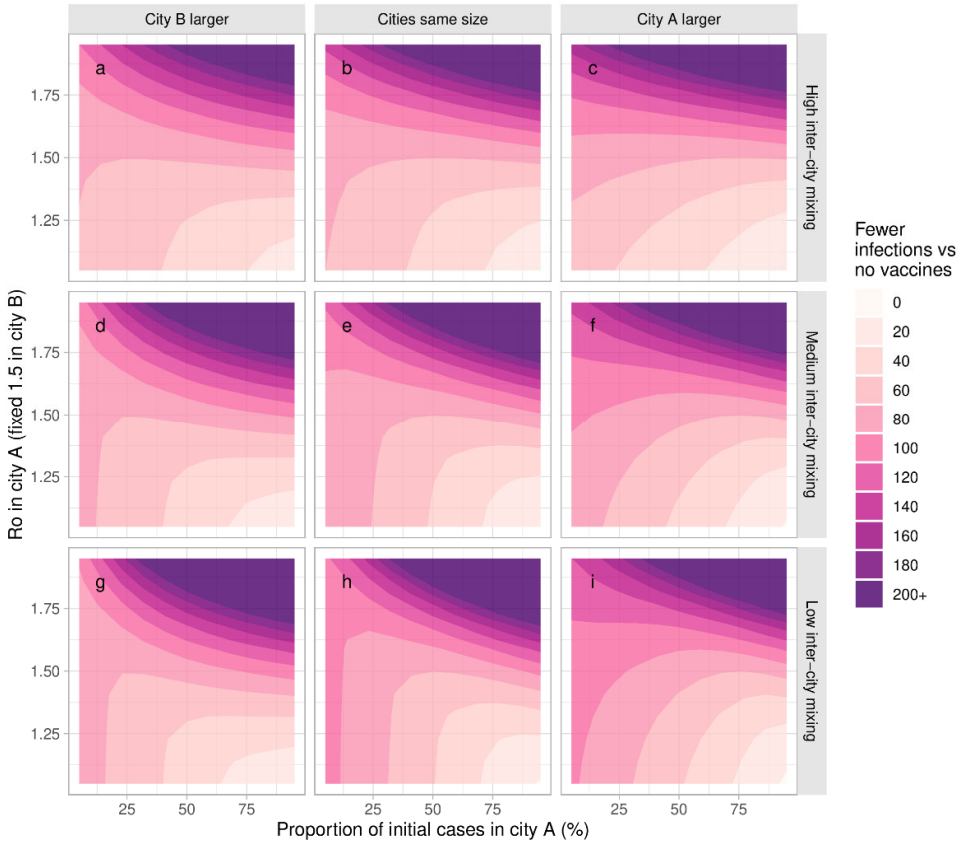

Figure B.2. Absolute fewer infections under optimal vaccine allocation versus no vaccination

R_0 in city A varies via the sexual activity among the higher risk group in city A. Optimal vaccine allocation is defined as fewest cumulative infections by day 90. The larger city is 3 times the size of the other city. High, medium, low inter-city mixing use ε_c = 0.8,0.9,0.95 respectively.

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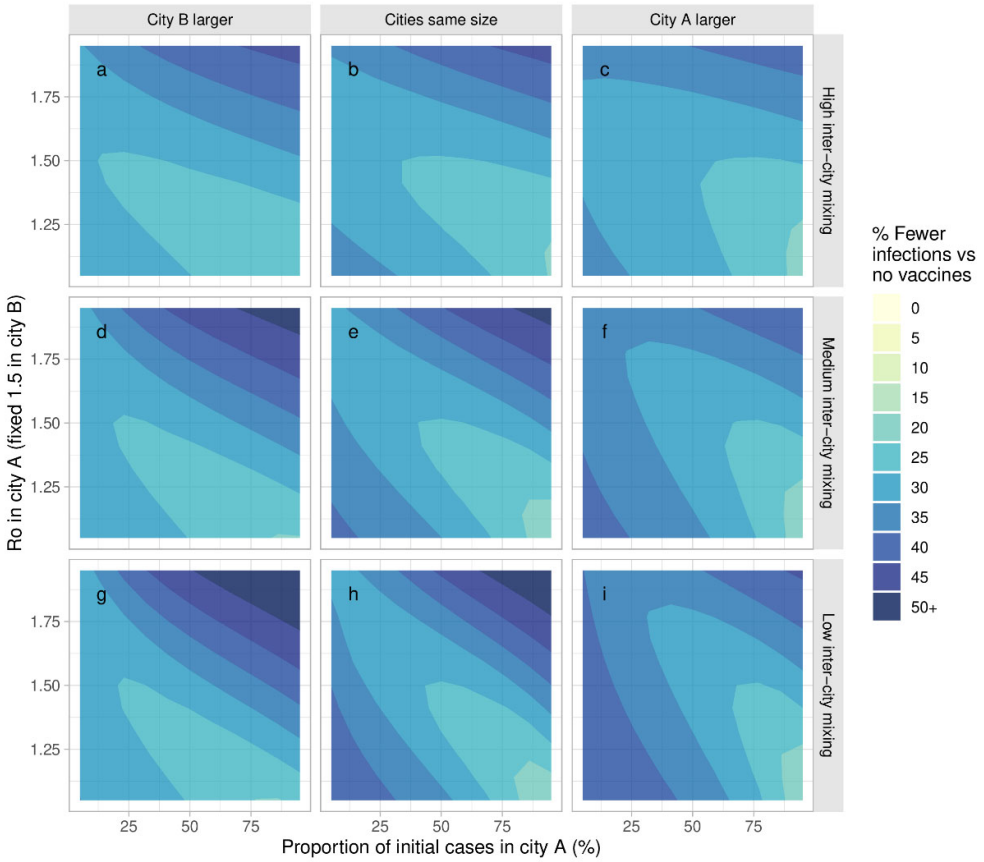

Figure B.3. Relative fewer infections under optimal vaccine allocation versus no vaccination

R_0 in city A varies via the sexual activity among the higher risk group in city A. Optimal vaccine allocation is defined as fewest cumulative infections by day 90. The larger city is 3 times the size of the other city. High, medium, low inter-city mixing use ε_c = 0.8,0.9,0.95 respectively.

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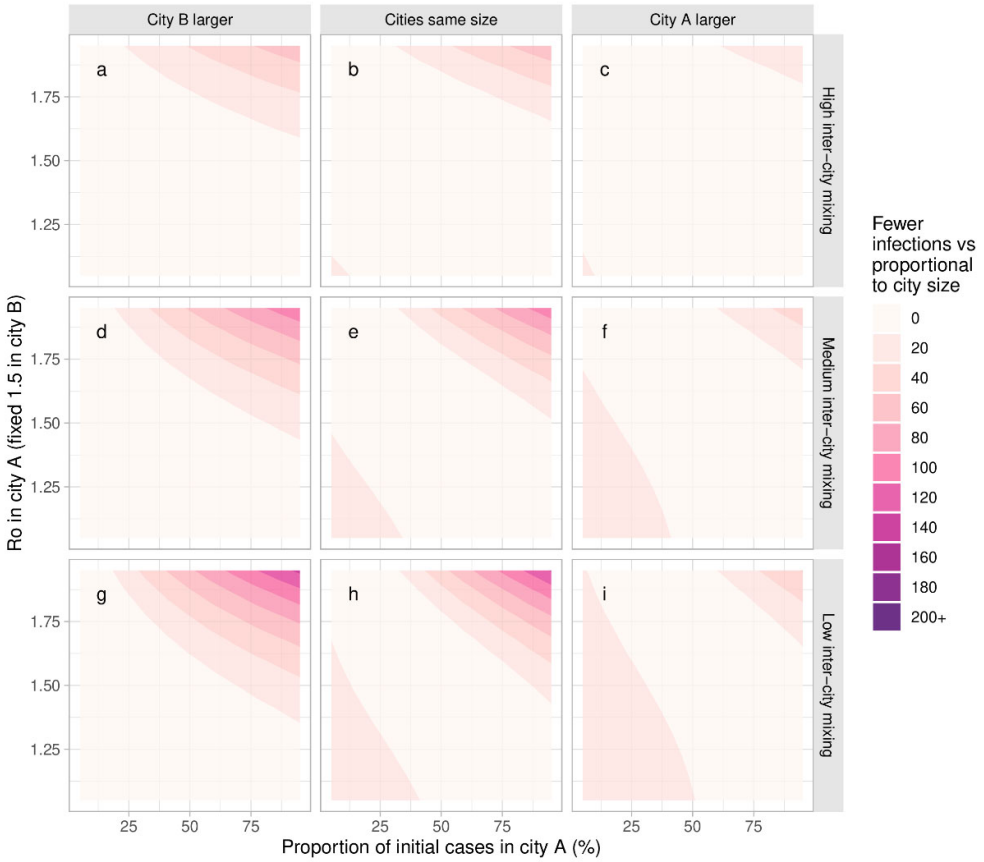

Figure B.4. Absolute fewer infections under optimal vaccine allocation versus allocation proportional to city size

R_0 in city A varies via the sexual activity among the higher risk group in city A. Optimal vaccine allocation is defined as fewest cumulative infections by day 90. The larger city is 3 times the size of the other city. High, medium, low inter-city mixing use ε_c = 0.8,0.9,0.95 respectively.

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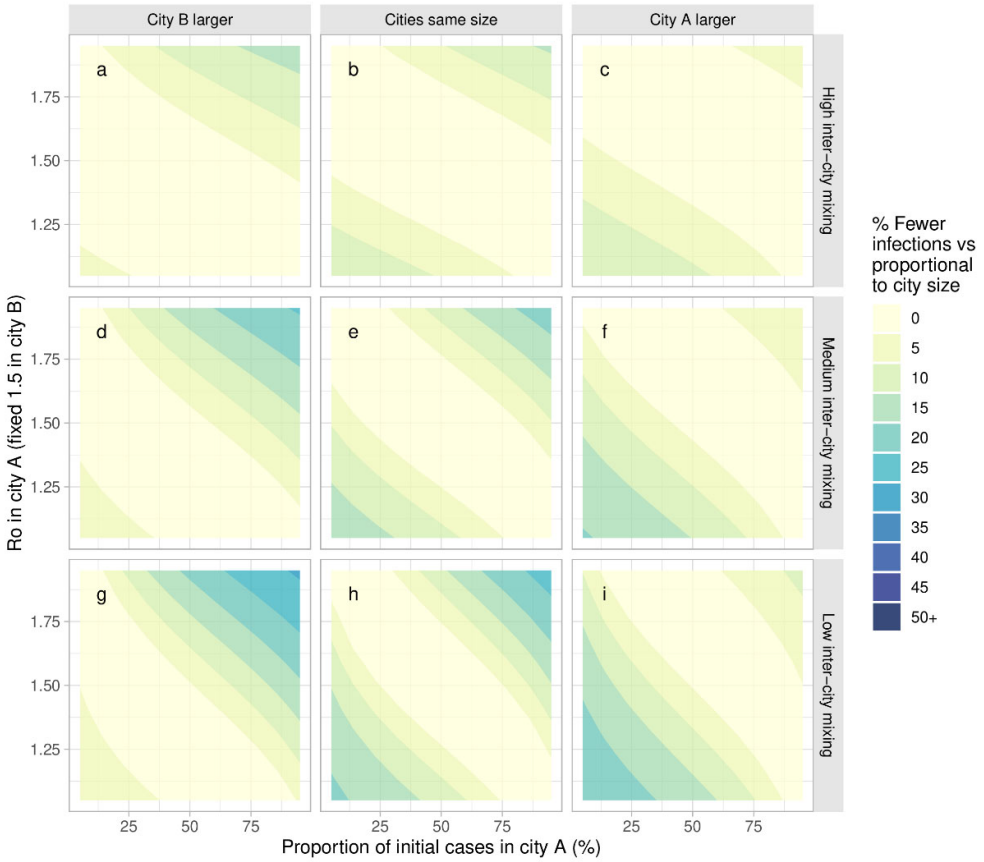

Figure B.5. Relative fewer infections under optimal vaccine allocation versus allocation proportional to city size

R_0 in city A varies via the sexual activity among the higher risk group in city A. Optimal vaccine allocation is defined as fewest cumulative infections by day 90. The larger city is 3 times the size of the other city. High, medium, low inter-city mixing use ε_c = 0.8,0.9,0.95 respectively.

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