# Disease and disaster: optimal deployment of epidemic control facilities in a spatially heterogeneous population with changing behaviour

Katy Gaythorpe *[1] and Ben Adams[1]

[1]Department of Mathematical Sciences, University of Bath, Bath, BA27AY, UK

February 19, 2016

**Keywords:** epidemic, natural disaster, metapopulation, environmental transmission, diarrhoea, behaviour, mathematical model

**Abstract**

Epidemics of water-borne infections often follow natural disasters and extreme weather events that disrupt water management processes. The impact of such epidemics may be reduced by deployment of transmission control facilities such as clinics or decontamination plants. Here we use a relatively simple mathematical model to examine how demographic and environmental heterogeneities, population behaviour, and behavioural change in response to the provision of facilities, combine to determine the optimal configurations of limited numbers of facilities to reduce epidemic size, and endemic prevalence. We show that, if the presence of control facilities does not affect behaviour, a good general rule for responsive deployment to minimise epidemic size is to place them in exactly the locations where they will directly benefit the most people. However, if infected people change their behaviour to seek out treatment then the deployment of facilities offering treatment can lead to complex effects that are difficult to foresee. So careful mathematical analysis is the only way to get a handle on the optimal deployment. Behavioural changes in response to control facilities can also lead to critical facility numbers at which there is a radical change in the optimal configuration. So sequential improvement of a control strategy by adding facilities to an existing optimal configuration does not always produce another optimal configuration. We also show that the pre-emptive deployment of control facilities has conflicting effects. The configurations that minimise endemic prevalence are very different to those that minimise epidemic size. So cost-benefit analysis of strategies to manage endemic prevalence must factor in the frequency of extreme weather events and natural disasters.

*K.A.M.Gaythorpe@bath.ac.uk

# 1 Introduction

Epidemics of water-borne infections, such as cholera and other diarrhoeal diseases, often follow flooding and other natural disasters when drinking water is contaminated and sewerage management is disrupted. It is mostly developing countries that are affected (Bouzid et al., 2013; Katsumata et al., 1998; Vollaard et al., 2004; Watson et al., 2007; WHO, 2006; Date et al., 2011; Ahern et al., 2005; Noji, 2000; WHO, 2006). The World Health Organisation (WHO) estimates that *Vibrio cholerae* alone causes approximately five million cases each year, leading to 120,000 deaths (WHO, 2014). Here we use a mathematical model to examine how demographic and environmental heterogeneities can be exploited to manage such epidemics as effectively as possible given limited resources.

Cholera is an environmentally transmitted infection. Susceptible individuals can be infected by ingestion of water or food contaminated with *V. cholerae*. Infected individuals shed bacteria, further contaminating the environment and perpetuating the transmission cycle. Five main control measures have been shown to limit or break this cycle: treatment of infected individuals, vaccination of susceptible individuals, provision of clean water, provision of sanitation, and environmental decontamination. Treatment of infected individuals with oral rehydration salts or antibiotics reduces the duration of infection and intensity of shedding. Vaccination of susceptible individuals provides broad but waning immunity to infection. Provision of clean water reduces contact between susceptible individuals and the contaminated environment. Provision of effective sanitation reduces the proportion of bacteria shed by infectious individuals that enter the environment. Decontamination reduces the lifespan of bacteria in the environment (Andrews and Basu, 2011; Mwasa and Tchuenche, 2011; Neilan et al., 2010; Eisenberg et al., 2013; Mukandavire et al., 2013; Tuite et al., 2011; Ochoche, 2013). Several mathematical modelling studies have examined the effects of these control measures on cholera epidemics. The epidemic risk in disease-free populations has been assessed using variants of the basic reproduction number. It has been shown that the risk is a product of social and economic factors with critical parameter values and population susceptibility dictating the possible epidemic behaviour. Sanitation affects the influence of the environmental reservoir on the risk (Codeço, 2001). The epidemic risk may be reduced most effectively by applying control strategies concurrently, rather than individually (Mwasa and Tchuenche, 2011), and targeting particular groups in heterogeneous populations (Eisenberg et al., 2013). Assessment of the endemic disease burden has shown that decontamination can be an effective control measure but may be insufficient to eradicate cholera if shed and contact rates are high (Ochoche, 2013). Assessment of the disease burden of a single epidemic has aimed to quantify the incidence reduction achievable through the provision of clean water, vaccination or antibiotics (Andrews and Basu, 2011). It has been shown that the ideal combination of control strategies depends on characteristics such as the ratio of asymptomatic to symptomatic cases, the average recovery rate and the duration of immunity (Neilan et al., 2010).

Mathematical modelling studies have also examined how cholera epidemics are affected by spatial structure and other heterogeneities in the population or environment. It has been shown that heterogeneities in clean water provision and sanitation affect outbreak severity at local and global scales (Mari et al., 2012; Njagarah and Nyabadza, 2014) and models with spatial heterogeneity predict the development of cholera epidemics better than homogeneous models (Mari et al., 2015). Models indicate that the hydrological network topology strongly affects the speed of the epidemic wave front as the disease propagates Bertuzzo et al. (2007, 2010), and can result in transmission

bottlenecks (Shuai et al., 2013; Shuai and Driessche, 2014). Human migration has been shown to be important for inter-catchment bacterial transport (Mari et al., 2012) and determining how best to allocate health care resources (Rinaldo et al., 2012). Here we contribute to understanding how human behaviour and population structures combine to influence the management of cholera by examining the effects of human movement, city structure and subpopulation heterogeneities on the optimal deployment of control facilities in endemic and epidemic settings. We model disease transmission in a large city with a basic spatial structure that accommodates heterogeneities in population density or clean water provision. We consider an epidemic associated with a natural disaster such as a flood and examine where, with respect to the heterogeneities, a limited number of control facilities should be deployed to minimise the number of infections. We show that the optimal distribution of control facilities depends on whether disease is absent or endemic before the perturbation, and what facilities are available. We also show that, when disease is endemic, the optimal pre-emptive deployment of control facilities to reduce the lifetime infection risk under endemic circulation is diametrically opposed to the optimal deployment for reducing epidemic size in the event of a perturbation.

### 1.1 Mathematical model

Our model framework is motivated by the archetypal structure of a developing world city (Potter and Lloyd-Evans, 1998): a central hub is surrounded by residential and industrial areas with population densities and the provision of services such as sanitation determined by the availability of transport links into the centre. We model this arrangement as a metapopulation structured into five patches in a star formation; a central patch connected to four peripheral patches (Figure 1). Individuals reside in a given patch but also interact with the environment of some other patches as a result of habitual travel. Residents of peripheral patches also interact with the environment of the central patch. Residents of the central patch also interact with the environment of all the peripheral patches. There is no direct bacterial transport as we consider human movement to be more important at the city scale and wish to focus on its impact. All patches are assumed to be of equal area. However, patches may be heterogeneous with respect to either the size of the resident population (effectively population density since area is constant), or the rate at which people in the patch come into contact with the environment (a measure of sanitation provision). When population density is heterogeneous the total population is divided between the five patches such that $\frac{1}{5}$ resides in the centre and $\frac{4}{5}$ reside in the peripheral patches, distributed non-uniformly as detailed in Table 1. When environmental contact rates are heterogeneous, the rates in the peripheral patches are distributed as detailed in Table 1, and the rate in the centre is the average of the peripheral rates. When densities or contact rates are homogeneous, each patch is assigned the average value of the heterogeneous distribution. A control facility provides either treatment or decontamination. Facilities may be assigned to some patches. Individuals are grouped according to the patch in which they are resident and their infection status. State variables $S_j$, $I_j$, $T_j$, $R_j$ describe the total number of susceptible, infected, treated and recovered individuals that are residents of patch $j$ where $j \in \{c, 1, 2, 3, 4\}$ indexes the central hub and each of the four peripheral patches. Additional state variables $B_j$ describe the concentration of bacteria in the environment in patch $j$.

The population is assumed to be at demographic equilibrium. The per capita birth and death rates are both $\mu$, and the size of the population resident in patch $j$ is $N_j$. The movement of people

couples patches. The nature of the coupling between patches $i$ and $j$ is modelled with a single parameter $\sigma_{ij}$ which weights the interaction a resident of patch $i$ has with patch $j$. This parameter reflects the tendency of people to be in each patch, summarising the fraction of people that travel together with the frequency and duration of their visits. The parametrisation of coupling terms such as these can be achieved by a decomposition using a gravity model (Chao et al., 2011; Gatto et al., 2012; Mari et al., 2015, 2012; Rinaldo et al., 2012; Tuite et al., 2011). Here, however, we wish to maintain a simpler model structure in order to focus on specific effects. Therefore, for individuals resident in patch $j \in \{c, 1, 2, 3, 4\}$ that are uninfected, or infected but treated, i.e. in states $S_j, T_j$ or $R_j$, interaction with their residential patch is weighted $\sigma_{jj} = \sigma$ and interaction with all other patches combined is weighted $1 - \sigma$. For residents of peripheral patches $j = 1, .., 4$ all of this interaction occurs in the centre patch. So $\sigma_{jc} = 1 - \sigma$. For residents of the centre patch $c$ the interaction is divided equally between the peripheral patches. So $\sigma_{cj} = \frac{1}{4}(1 - \sigma)$.

The interaction weights for individuals resident in patch $j \in \{c, 1, 2, 3, 4\}$ that are infected but not treated, i.e. in state $I_j$, are modified to reflect the inclination of such individuals to seek treatment. Let $\chi_1 < 1$ be an inertia weight reflecting the disinclination of an infected individual to move away from a location where treatment is available. Let $\chi_2 > 1$ be an animation weight reflecting the inclination to move toward a location, within an individual's habitual travel area, where treatment is available. Then, for individuals resident in a peripheral patch $j$ that are in state $I_j$, interaction with their residential patch is weighted $\sigma^I_{jj}$ where

$$\sigma^I_{jj} = \begin{cases} \frac{\sigma\chi_2}{\sigma\chi_2+(1-\sigma)\chi_1} & \text{if } j \text{ has a treatment facility and } c \text{ does not} \\ \frac{\sigma\chi_1}{\sigma\chi_1+(1-\sigma)\chi_2} & \text{if } j \text{ does not have a treatment facility and } c \text{ does} \\ \sigma & \text{if both } j \text{ and } c \text{ have treatment facilities, or neither do.} \end{cases} \tag{1}$$

In the same way as before $\sigma^I_{jc} = 1 - \sigma^I_{jj}$. Equation (1) adjusts the basic interaction weight of uninfected individuals $\sigma$ according to the infection related inertia and animation weights $\chi_1$ and $\chi_2$. It has the desirable characteristics $\sigma_{jj} \to 1$ as $\chi_2 \to \infty$ if there is a treatment facility in $j$ but not $c$, $\sigma_{jj} \to 0$ as $\chi_2 \to \infty$ if there is a treatment facility in $c$ but not $j$, $\sigma_{jj} = 0$ if $\chi_2 = 0$ and $\sigma_{jj} = \sigma$ if $\chi_1 = \chi_2 = 1$ and treatment facilities do not motivate any inertia or animation.

For infected residents of the central patch the weighting is complicated by the fact that treatment may only be available in some of the peripheral patches. Let the proportion of peripheral patches with treatment facilities be $\rho$. Then, for individuals resident in the centre patch $c$ that are in state $I_c$, interaction with their residential patch is weighted $\sigma^I_{cc}$ where

$$\sigma^I_{cc} = \begin{cases} \dfrac{\sigma\chi_2}{\sigma\chi_2 + (1-\sigma)(\rho\chi_2 + (1-\rho)\chi_1)} & \text{if } c \text{ and a proportion } \rho \text{ of peripheral patches have treatment facilities} \\ \dfrac{\sigma\chi_1}{\sigma\chi_1 + (1-\sigma)(\rho\chi_2 + (1-\rho)\chi_1)} & \text{if a proportion } \rho \text{ of peripheral patches have treatment facilities but } c \text{ does not} \\ \sigma & \text{else.} \end{cases} \tag{2}$$

Equation (2) adjusts the basic interaction weight of uninfected individuals $\sigma$ according to the infection related inertia and animation weights $\chi_1$ and $\chi_2$, scaled by the proportion of peripheral

patches with treatment facilities. These scaled weights also give interaction weights outside of the residential patch $\sigma^I_{cj}$ where

$$\sigma^I_{cj} = \begin{cases} \dfrac{(1-\sigma)\rho\chi_2}{\sigma\chi_2 + (1-\sigma)(\rho\chi_2 + (1-\rho)\chi_1)} & \text{if } c \text{ and } j \text{ have treatment facilities} \\ \dfrac{(1-\sigma)(1-\rho)\chi_1}{\sigma\chi_2 + (1-\sigma)(\rho\chi_2 + (1-\rho)\chi_1)} & \text{if } c \text{ has a treatment facility and } j \text{ does not} \\ \dfrac{(1-\sigma)\rho\chi_2}{\sigma\chi_1 + (1-\sigma)(\rho\chi_2 + (1-\rho)\chi_1)} & \text{if } c \text{ does not have a treatment facility and } j \text{ does} \\ \dfrac{(1-\sigma)(1-\rho)\chi_1}{\sigma\chi_1 + (1-\sigma)(\rho\chi_2 + (1-\rho)\chi_1)} & \text{if neither } c \text{ nor } j \text{ have treatment facilities.} \end{cases} \tag{3}$$

Equations (2) and (3) have the desirable property that, under equivalent conditions, the interaction weights of residents of the central patch are the same as those of residents of a peripheral patch. If all the peripheral patches have treatment facilities, or none of them do, the residential/non-residential interaction weights for residents of the central patch are equal to the equivalent weights given by equation (1) for residents of a peripheral patch when there is a treatment facility in the centre but not in the residential patch, or vice versa.

While interacting with the environment of patch $j$, susceptible individuals come into contact with the bacterial reservoir at rate $\beta_j$ and each contact leads to infection with probability $\frac{B_j}{\kappa+B_j}$ where $\kappa$ is the half-saturation constant. So the force of infection $\mathcal{F}_c$ experienced by residents of the central patch is composed of terms representing exposure in patch $c$, and exposure in each peripheral patch $i$

$$\mathcal{F}_c = \beta_c \frac{B_c}{\kappa + B_c}\sigma + \sum_j \beta_j \frac{B_j}{\kappa + B_j}\frac{(1-\sigma)}{4}. \tag{4}$$

Similarly, the force of infection experienced by residents of peripheral patch $j$, $\mathcal{F}_j$ is composed of terms representing exposure in patch $c$, and exposure in patch $j$:

$$\mathcal{F}_j = \beta_c \frac{B_c}{\kappa + B_c}(1-\sigma) + \beta_j \frac{B_j}{\kappa + B_j}\sigma. \tag{5}$$

Infected individuals recover at rate $\gamma$ or, while they are interacting with a patch with a treatment facility, receive treatment at rate $\xi$. So infected residents of the central patch are treated at rate $\mathcal{H}_c$, and residents of peripheral patch $j$ are treated at rate $\mathcal{H}_j$ where

$$\begin{aligned} \mathcal{H}_c &= \sigma^I_{cc}\xi_c + \sum_j \sigma^I_{cj}\xi_j \\ \mathcal{H}_j &= \sigma^I_{jc}\xi_c + \sigma^I_{jj}\xi_j \end{aligned} \tag{6}$$

and

$$\xi_i = \begin{cases} \xi \text{ if patch } i \text{ has a treatment facility} \\ 0 \text{ if patch } i \text{ does not have a treatment facility.} \end{cases} \tag{7}$$

Treated individuals recover faster than untreated individuals, at rate $\alpha\gamma$ where $\alpha > 1$. Infected individuals, including those that have been treated but have not yet recovered, shed bacteria at rate $\eta$. So the total rates at which bacteria are shed into the central patch, $\mathcal{G}_c$, and into peripheral patch $j$, $\mathcal{G}_j$, are composed of terms representing the contributions of residents and non-residents.

$$\begin{aligned} \mathcal{G}_c &= \left( \sigma^I_{cc} I_c + \sum_j \sigma^I_{jc} I_j + \sigma T_c + \sum_j (1-\sigma) T_j \right) \eta \\ \mathcal{G}_j &= \left( \sigma^I_{cj} I_c + \sigma^I_{jj} I_j + \frac{(1-\sigma)}{4} T_c + \sigma T_j \right) \eta. \end{aligned} \tag{8}$$

Note that this differs from the model proposed by Mari et al. (2015), where non-residents can be infected by the bacterial reservoir, but do not contribute to it.
Bacteria in the environment degrade naturally at rate $\zeta$ and are removed by decontamination at rate $\theta_i$ where

$$\theta_i = \begin{cases} \theta \text{ if patch } i \text{ has a decontamination facility} \\ 0 \text{ if patch } i \text{ does not have a decontamination facility.} \end{cases} \tag{9}$$

A flow diagram for the system is shown in Figure 1. The epidemiological dynamics for residents of patch $i \in \{c, 1, 2, 3, 4\}$ are given by

$$\begin{aligned} \dot{S}_i &= \mu N_i - \mathcal{F}_i S_i - \mu S_i \\ \dot{I}_i &= \mathcal{F}_i S_i - (\gamma + \mathcal{H}_i + \mu) I_i \\ \dot{T}_i &= \mathcal{H}_i I_i - (\alpha\gamma + \mu) T_i \\ \dot{R}_i &= \alpha\gamma T_i + \gamma I_i - \mu R_i \\ \dot{B}_i &= \mathcal{G}_i - (\zeta + \theta_i) B_i. \end{aligned} \tag{10}$$

Parameter values are given in Table 1. The basic reproduction number for the system is straightforward to calculate using the Next Generation Matrix method (Diekmann et al., 2010; Diekmann and Heesterbeek, 2000; Heffernan et al., 2005; Arino and Van den Driessche, 2003; Arino and van den Driessche, 2006). With the parameter values given in Table 1, and when no control facilities are deployed, the 'disease-free' parameter sets give $R_0$ around 0.9 before the 'flood' perturbation, and around 1.8 during it. Hence the disease-free equilibrium is stable in the unperturbed system, and unstable in the perturbed system. The 'endemic' parameter sets give $R_0$ around 2.8 in the unperturbed system and 5.6 in the perturbed system. So the disease-free equilibrium is unstable in these cases. We have not made an analytic assessment of the stability of the endemic equilibrium, but numerical convergence of the ordinary differential equations to these points suggests they are stable for all the parameters sets we considered such that $R_0 > 1$. Further details of the $R_0$ calculation and additional values for the system can be found in the Supplementary Information, Table S1.

| Parameter | Meaning | Value |
|---|---|---|
| $N$ | Total population | $7 \times 10^5$ |
| $N_j$ | Homogeneous resident population, all patches (*) | $1.4 \times 10^5$ |
| $N_j$ | Heterogeneous resident population, patch $j = [c, 1, 2, 3, 4]$ (*) | $[1.4, 0.98, 1.26, 1.54, 1.82] \times 10^5$ |
| $\mu$ | Birth/death rate, average lifespan 70 years | $4 \times 10^{-5}$ |
| $\sigma$ | Residential interaction weight, non-infected | 0.67 |
| $\chi_1$ | Inertia due to treatment facility | 0.2 |
| $\chi_2$ | Animation due to treatment facility | 2 |
| $\beta_j$ | Homogeneous contact rate with environment, all patches, endemic (*) | 1 |
| $\beta_j$ | Homogeneous contact rate with environment, all patches, disease-free (*) | 0.1 |
| $\beta_j$ | Heterogeneous contact rate with environment, patch $j = [c, 1, 2, 3, 4]$, endemic (*) | $[1, 0.7, 0.9, 1.1, 1.3]$ |
| $\beta_j$ | Heterogeneous contact with environment, patch $j = [c, 1, 2, 3, 4]$, disease-free (*) | $[0.1, 0.07, 0.09, 0.11, 0.13]$ |
| $\kappa$ | Half-saturation constant for transmission | $2.5 \times 10^7$ |
| $\xi$ | Treatment rate | 0.5 |
| $\gamma$ | Recovery rate, average infection duration 5 days | 0.2 |
| $\alpha$ | Recovery rate enhancement due to treatment | 3 |
| $\eta$ | Unperturbed bacterial shedding rate, scaled by reservoir volume | 17.86 |
| $\zeta$ | Natural bacterial degradation rate | 0.25 |
| $\theta$ | Bacterial decontamination rate | 0.5 |

Table 1: Parameter values used throughout the analysis unless stated otherwise. (*) indicates a parameter set option. There are homogeneous and heterogeneous population size $N_j$ and contact rate $\beta_j$ parametrisations. In addition there are contact rate parametrisations such that the disease-free equilibrium is stable, or the endemic equilibrium is stable. All rates are per day. The values of $\eta, \beta, \kappa, \gamma, \eta, \theta$ are based on those used in previous studies (Chao et al., 2011; Codeço, 2001; Gatto et al., 2012; Mari et al., 2012; Mukandavire et al., 2011; Piarroux et al., 2011).

## 1.2 Methods

We consider the dilemma faced by healthcare planners and disaster response teams. We wish to determine where, in a city structured by commuting patterns, population density and clean water provision, a limited number of control facilities should be deployed to minimise the impact of an infectious disease epidemic following a perturbation in transmission rates. We consider situations in which, prior to the perturbation, disease is endemic or the population is disease-free. The control facilities are deployed reactively, as soon as the flood occurs, with the objective of minimising the epidemic size. In the case of endemic disease we also consider deployment of control facilities pre-emptively, in the unperturbed system, with the objective of minimising the lifetime infection risk and contrast this with the configurations that minimise epidemic size in the event of a perturbation.

We use our model to simulate the breakdown in water management following a natural disaster. We take a system at a stable equilibrium, either disease-free or disease-endemic, as determined by the environmental contact rate parameter set $\beta_j$. We then simulate a flood by perturbing these contact rates, and the rate at which bacteria enter the environment $\eta$. These parameters are doubled as shown in Figure 2. For initially disease-free populations, the perturbation is accompanied by a small number of infections (a total of 7 infected individuals distributed in proportion to the population sizes of each patch). The perturbation lasts for 50 days, after which $\beta_j$ and $\eta$ return to their previous values. The increase in transmission leads to an epidemic that begins to subside when the perturbation comes to an end or the susceptible population is exhausted.

In terms of epidemic management we define the optimal configuration of the available control facilities to be the one that minimises the epidemic size following the perturbation. The epidemic size is, for the purposes of this analysis, defined as the total number of new infections between the start and end of the perturbation, a duration of 50 days, in excess of the number that would have occurred over the same time period in the unperturbed system. We also considered the epidemic size over a period of 365 days; the optimal configurations did not change. We find the number of new infections by numerical integration of system (10). For reactive deployment the initial condition is the equilibrium state (disease-free or endemic) with no control facilities present. For pre-emptive deployment it is the equilibrium state with the given configuration of facilities present. We consider configurations of one to four treatment facilities, of one to four decontamination facilities and of one to nine facilities composed of any combination of up to five treatment facilities and up to five decontamination facilities. We find the optimal configurations by exhaustive search. We use a metric $\delta$ to locate these optimal configurations in the 'operating space' of all possible configurations. The metric is defined as follows. Let $Z_C$ be the size of the perturbation-induced epidemic under any given control facility configuration $C$. Let $Z_0$ and $Z_F$ be the corresponding epidemic sizes when there are, respectively, no control facilities, and a full complement of control facilities. A full complement means five treatment or five decontamination facilities when only one type is used, or five treatment and five decontamination facilities when both types are used. Then we define $\delta$ to be the reduction in epidemic size achieved with configuration $C$ relative to the reduction achieved with a full complement of facilities:

$$\delta = \frac{Z_0 - Z_C}{Z_0 - Z_F} \tag{11}$$

If $\delta = 0$, configuration $C$ is the same as not making any intervention. If $\delta = 1$, configuration $C$ is as effective as a full complement of facilities. If $\delta > 1$, configuration $C$ is more effective than a full complement of facilities.

## 1.3 Results

### 1.3.1 Reactive deployment

We first consider the optimal deployment of decontamination or treatment facilities at the moment the perturbation begins. The patches in which control facilities are deployed can have a notable impact on the epidemic size. For example Figure 3 shows infection prevalence over time following the perturbation when population density is heterogeneous, disease is endemic and a single decontamination facility is reactively deployed to each of the five possible patches. In this case it is optimal to locate one decontamination facility in the centre patch. This leads to an epidemic that

is 9.2 % smaller than the least effective deployment.

Table 2 summarises the reactive configurations of control facilities that are optimal, or nearly optimal, in terms of minimising epidemic size. These are the same for heterogeneous densities or contact rates. The top four rows summarise the general rules for one to four facilities of the same type. The optimal, or nearly optimal, configuration of decontamination facilities is to place one in the centre and then prioritise peripheral patches with the highest population densities or environmental contact rates. The situation for treatment facilities is more complicated. If the system is initially at disease-free equilibrium and one or two facilities are available, the first is placed in the centre patch and a second is placed in the peripheral patch with the highest density or contact rate. However, if three or four facilities are available the optimal configuration switches such that the central patch is omitted and facilities are located in the peripheral patches with highest contact rate or density. This switch results in a markedly lower epidemic size than adding additional facilities to the optimal configuration of two facilities. If the system is initially at endemic equilibrium the situation is similar, but the switch to the configuration that omits the centre patch only occurs when four facilities are available. The bottom row shows the general rule for one to nine facilities chosen from a pool of five treatment and five decontamination facilities. Initially decontamination and treatment facilities are placed in the central patch. For the disease-free parameter sets, this deployment is sufficient to reduce $R_0$ below 1 even after the perturbation. Hence all configurations of two ore more facilities that include this dual deployment to the centre prevent an epidemic and are effectively indistinguishable using our method of ranking by epidemic size. For the endemic parameter sets, however, the $R_0$ is greater than 1 after the perturbation for all facility deployments. In this case, if more than two facilities are available, decontamination facilities are placed in the peripheral patches, prioritising those with the highest population densities or contact rates. Then treatment facilities are placed in the peripheral patches, prioritising those with the lowest population densities or contact rates. However, if nine control facilities are available the optimal configuration omits the treatment facility from the central patch. In a few cases, as detailed in Table 2, the configurations determined from these rules are not quite optimal; an alternative configuration leads to a marginally smaller epidemic size. However, these deviations are small and sensitive to the parametrisation details, as detailed in the Supplementary Information Tables S2 and S4). So the rules we have described are good indicators of configurations that are optimal, or very nearly optimal.

The numerical values in Table 2 indicate, for single facility types and heterogeneous densities, the impact on the epidemic size of the optimal configuration relative to a full complement of facilities according to our metric $\delta$ (equation 11). If the system is initially at endemic equilibrium, a single treatment facility in the central patch is very effective in reducing the epidemic size but reasonable further reductions can be achieved by adding more facilities to the periphery. Note, however, that it is more effective to deploy four treatment facilities in the optimal configuration than it is to deploy five i.e. a facility in every patch. A single decontamination facility in the central patch has a modest impact and a steady incremental benefit accrues from each additional facility up to a total of five. If the system is initially disease-free, a single treatment facility in the central patch achieves is almost as effective as deploying facilities to all five patches. Adding further facilities to the periphery has a very small impact. A single decontamination facility in the central patch is very effective, there is a non-negligible return from adding one further facility to the periphery, but further facilities have little impact. When contact rates are heterogeneous or two

facility types are deployed, the general patterns of the single facility type analysis carry through (see the Supplementary Information Table S6). As noted above, if the system is initially disease-free placing treatment and decontamination facilities in the central patch pushes the basic reproduction number of the perturbed system below one. So all configurations that include this deployment entirely prevent an epidemic and are indistinguishable.

### 1.3.2 Pre-emptive deployment

We now consider the deployment of treatment and decontamination facilities in advance of any perturbation. When the system is at disease-free equilibrium before the perturbation it makes no difference whether control facilities are deployed reactively or pre-emptively, so the optimal pre-emptive configurations are as given in Table 2. However, when the system is at endemic equilibrium, the control facilities affect the steady-state prevalence before the perturbation as well as the epidemic that follows it. In this case a natural objective of a control facility deployment is to minimise the lifetime infection risk in the absence of a perturbation. But this objective may be in conflict with the objective of minimising epidemic size given a perturbation. We examine this tension by finding the configurations that are optimal in each sense. We quantify the endemic risk as the lifetime probability of infection $1-S^*/N$ where $S^*$ is the total susceptible population at equilibrium.

Table 3 shows that the objective of minimising lifetime epidemic risk under endemic circulation is in direct opposition to the objective of minimising epidemic size in the event of a perturbation. Any deployment of control facilities reduces the lifetime infection risk, but this increase in the size of the steady-state susceptible population also increases the epidemic size in the event of a perturbation. So the 'optimal' configuration with respect to epidemic size is the one that leads to the smallest increase in the number of infections, rather than the largest decrease. The top four rows show the configurations for one to four facilities of the same type. In order to minimise lifetime infection risk, the required configurations are in broad agreement with the rules for reactively placed facilities: generally prioritise the centre followed by high density peripheral patches. In order to minimise epidemic size, one to three decontamination or treatment facilities are all are located in the peripheral patches, prioritising those with the lowest population densities or contact rates. For four decontamination facilities this rule is extended and no facility is placed in the centre patch. For four treatment facilities the configuration switches to one in which a facility is placed in the centre patch, and no facility is placed in the peripheral patch with the lowest density. This configuration is markedly better than omitting the centre patch. The bottom two rows of Table 3 show the optimal configurations of both facility types. Again there is there is a sharp distinction between the rules for pre-emptively placed configurations to minimise infection risk, and the rules for minimising epidemic size.

The numerical values in Table 3 indicate, for single facility types and heterogeneous population densities, the impact on the epidemic size, or the lifetime infection risk, of the optimal configuration relative to a full complement of facilities according to our metric $\delta$. Values for heterogeneous contact rates and two facility types are given in the Supplementary Information, Table S7. Each additional decontamination facility returns a fairly steady incremental reduction in the lifetime infection risk. A single treatment facility reduces the lifetime infection risk substantially, and additional facilities return small incremental reductions. With regards epidemic size, recall that the largest epidemics occur under a full complement of control facilities. So $\delta$ is a measure of the cost in terms of the

size of a perturbation-induced epidemic of a particular configuration; lower values are better. Up to four decontamination facilities can be deployed to the peripheral patches with relatively limited increases in the epidemic size, but the deployment of a fifth facility to the central patch leads to a large increase. In contrast, each treatment facility that is deployed results in a steady incremental increase in the epidemic size. These broad trends remain when both facility types are deployed.

### 1.4 Discussion

We have examined how structured heterogeneities in population density and the rate of contact with the contaminated environment combine with a behavioural response to affect the optimal deployment of treatment and decontamination facilities to limit epidemics of environmentally transmitted infections such as cholera. Our model was based on a star, or hub-and-spokes, framework motivated by the archetypal structure of developing world cities. This abstraction omits direct connections between peripheral patches in the interests of simplicity. Introducing these additional edges requires a systematic framework to record and determine which peripheral patches are connected, with what weights and with what dependence on the distribution of treatment facilities. This substantial increase in model complexity will make it more difficult to extract general rules from the output. We anticipate, however, that peripheral connectivity would have the effect of increasing mixing in the population, diluting the impacts of spatial structure and other heterogeneities. The simple hub and spokes structure of our model, with heterogeneous patches coupled through people's habitual movement, cannot be expected to produce detailed predictions or specific control recommendations for real world systems. The necessity of numerical analysis means that we cannot offer a succinct formula encapsulating the answer in full generality. Instead this study offers fundamental insights into the problem of epidemic control in structured systems that provide support for real-world decision making, informing the construction and analysis of detailed models for specific circumstances. Sensitivity analysis, detailed in the Supplementary Information Figures S1 - S10, suggests that our results are robust to variation in most model parameters. The key parameters that do affect our results are indicative of the mechanisms behind the dynamics and are discussed in detail below.

We have shown that, even in our relatively simple system, the dynamics and the decision making can be complex. Four factors stand out. (1) The behavioural response of the population to control facilities can affect how they should be deployed. Optimal configurations of decontamination facilities are different to those of treatment facilities in a large part because infected individuals were attracted to locations where treatment is available. (2) Adding to an existing optimal configuration of control facilities does not necessarily lead to another optimal configuration. There are critical values of the number of facilities to be deployed at which optimisation requires a switch to a markedly different configuration. (3) In some cases a single optimally placed control facility can be almost as effective as deploying control facilities in all locations, and four treatment facilities may be better than five. (4) Pre-emptive control facility deployments can have conflicting consequences. The configurations that minimise endemic prevalence are very different to those that minimise epidemic size in the event of a transmission perturbation. We now explore the mechanisms behind some of these observations.

The basic principle guiding the location of control facilities is that they should be placed where they will benefit the most people. But this patch is not always straightforward to identify. For reactive deployment we found that, if only decontamination facilities are used, one should be deployed

to the centre and then the peripheral patches with the highest density or contact rate should be prioritised. The centre is important because the star-structured coupling means that a large proportion of the total population has some exposure to the environment of the central patch. However, if the coupling strength is reduced (i.e. the residential exposure weight $\sigma$ is increased) the central patch becomes less important. If the population densities and contact rates are homogeneous a decontamination facility always benefits the most people if placed in the central patch; the proportion of residents that benefit from a decontamination facility is the same for all patches, but the proportion of non-residents that benefit is four times greater in the central patch than in any of the peripheral patches. However, if the population densities or contact rates are heterogeneous and the residential exposure weight $\sigma$ is sufficiently large, placing the decontamination facility in the peripheral patch with the highest population density or underlying contact rate may benefit more people than placing it in the centre. Figure 4 shows this mechanism in action. Epidemic size is plotted as a function of the residential exposure weight for systems with one decontamination facility. When the residential exposure weight is small it is clearly best to place the decontamination facility in the centre. When the residential exposure weight is large preference switches to the peripheral patch with the highest population density. When the residential exposure weight is close to 1, so there is almost no non-residential exposure, even the peripheral patch with the second highest population density is a better location for a decontamination facility than the centre.

We found that, if only treatment facilities are used, one should be deployed to the centre and then the peripheral patches with the lowest density or contact rate should be prioritised if one, two or, in some cases, three facilities are available. But if more facilities are available, the deployment should omit the centre. The dominant factor governing the optimal configurations of treatment facilities is the attraction of infected people to these facilities, summarised in the inertia and animation weights $\chi_1, \chi_2$. If there is no attraction ($\chi_1 = \chi_2 = 1$) then the key factor is again the residential exposure weight $\sigma$, and the optimal configurations of treatment and decontamination facilities are similar. If infected people are attracted to treatment facilities the net benefit of placing one in any particular patch is a trade-off between accessibility and contamination. The centre patch may be a good place for a treatment facility because people from all the patches in the system can benefit from it. However, these people also shed bacteria into the environment while waiting for treatment. The centre patch is a hub for susceptible people, as well as those that are infected. If infected individuals are strongly attracted to a treatment facility ($\chi_2$ large and/or $\chi_1$ small) in the centre, the consequences of contaminating the hub may outweigh the benefits of accessibility. In this case it is preferable to omit the centre and place treatment facilities in the periphery. The limited access to peripheral patches means that a smaller proportion of the infected population benefit from the facility, but overall the susceptible population benefits from an 'auto-quarantine' effect whereby infected individuals are kept away from the hub and other patches with high population densities or underlying contact rates. It is this auto-quarantine effect that can result in a deployment of four treatment facilities being more effective than five at reducing epidemic size. When there are four facilities infected individuals show a preference for patches where treatment is available, when there are five facilities all patches are equally attractive.

Figure 5 shows the auto-quarantine mechanism in action. Epidemic size is plotted as a function of the inertia and animation rates, $\chi_1$ and $\chi_2$ (coupled such that $\chi_2 = 1 + 10(1 - \chi_1)$), for systems with two treatment facilities. When the $\chi_1, \chi_2$ are close to 1, so there is very weak attraction to treatment facilities, it is best to place the facilities in the centre and the peripheral patch with

highest population density (region A). This configuration provides access to treatment for the largest number of people, mainly in their residential patches. As $\chi_2$ increases and $\chi_1$ decreases, so treatment facilities become more attractive, it is clearly preferable to switch the peripheral facility away from the high density patch, although it does not make much difference where it is placed instead (region B). The attraction of infected people to treatment facilities means that residents of the high density peripheral patch without a facility access treatment in the centre patch. This is of direct benefit to those individuals, and also reduces contamination of their residential patch. It does, however, increase contamination in the centre patch. As $\chi_2$ increases and $\chi_1$ decreases further this contamination of the centre patch makes it preferable to omit the facility from the centre and focus on containing the contamination in the peripheral patches, prioritising those with the highest population density again in order to reach the largest residential populations (region C).

The trade-off between providing access to treatment and limiting contamination is also evident if we consider how the waiting time to treatment ($1/\xi$) affects the optimal configuration of treatment facilities. Figure 6 shows how the optimal location of a single treatment facility depends on the waiting time to treatment. When the waiting time is short it is best to place the facility in the centre as this provides access for the largest number of people. As the waiting time increases it becomes preferable to switch the facility first to the highest density peripheral patch, and then to peripheral patches with successively lower population densities. If infected individuals have to wait longer for treatment they cause more contamination in the patches where the treatment facilities are located. Moving the facility to locations with lower population density reduces access, but also reduces the overall transmission to the susceptible population.

Pre-emptive deployment of control facilities affects the lifetime infection risk under endemic circulation. It also affects the size of a perturbation-induced epidemic directly, by reducing transmission during the epidemic, and indirectly by altering the endemic state of the population prior to the perturbation. The configurations that minimise the lifetime infection risk at endemic equilibrium also minimise epidemic size under reactive deployment. However, under pre-emptive deployment all control facility configurations increase epidemic size compared with the uncontrolled system because they increase the total susceptible population at equilibrium. Consequently, the pre-emptive configurations that minimise endemic infection risk are among the least beneficial when it comes to minimising epidemic size. So, while the guiding principle remains to place the facilities where they will benefit the most people, the definition of benefit requires careful thought. In regions where extreme weather events or natural disasters are not uncommon, the deployment of facilities to manage endemic infections can be a double edged sword. The gains made in reducing endemic prevalence may be offset by more severe epidemics during periods of increased transmission.

## 2 Conclusion

It seems like a simple enough request: deploy these transmission control facilities where they will benefit the most people. But making the correct deployment requires careful analysis. Control measures that do not affect peoples' behaviour, such as decontamination in our analysis, should be deployed to the areas where the most people, be they residents or non-residents, are exposed to transmission. But control measures that do affect behaviour, such as treatment in our analysis, can lead to complex effects that are difficult to foresee. In these cases careful mathematical analysis is the only way to get a handle on the optimal deployment, and the mechanisms that govern it. Assessing

pre-emptive deployments in communities with endemic disease is complicated by conflicting effects on different time scales. Reducing endemic prevalence makes the population more vulnerable to larger epidemics in the event of a transmission perturbation. So cost-benefit analysis of strategies to manage endemic prevalence must factor in the frequency of extreme weather events and natural disasters. Cholera and other diarrhoeal diseases are the second largest cause of morbidity in children under the age of five years (WHO, 2015). The simple insights presented here are a step towards more effective control strategies in resource-limited situations.

## References


Mike Ahern, R Sari Kovats, Paul Wilkinson, Roger Few, and Franziska Matthies. Global health impacts of floods: epidemiologic evidence. *Epidemiologic Reviews*, 27(1):36–46, 2005.

Jason R Andrews and Sanjay Basu. Transmission dynamics and control of cholera in Haiti: an epidemic model. *The Lancet*, 377(9773):1248–1255, 2011.

Julien Arino and P Van den Driessche. A multi-city epidemic model. *Mathematical Population Studies*, 10(3):175–193, 2003.

Julien Arino and P van den Driessche. Disease spread in metapopulations. *Nonlinear Dynamics and Evolution Equations, Fields Inst. Commun*, 48:1–13, 2006.

E Bertuzzo, A Maritan, M Gatto, I Rodriguez-Iturbe, and A Rinaldo. River networks and ecological corridors: reactive transport on fractals, migration fronts, hydrochory. *Water Resources Research*, 43(4), 2007.

E Bertuzzo, R Casagrandi, M Gatto, I Rodriguez-Iturbe, and A Rinaldo. On spatially explicit models of cholera epidemics. *Journal of the Royal Society Interface*, 7(43):321–333, 2010.

Maha Bouzid, Lee Hooper, and Paul R Hunter. The effectiveness of public health interventions to reduce the health impact of climate change: a systematic review of systematic reviews. *PloS One*, 8(4):e62041, 2013.

Dennis L Chao, M Elizabeth Halloran, and Ira M Longini Jr. Vaccination strategies for epidemic cholera in Haiti with implications for the developing world. *Proceedings of the National Academy of Sciences*, 108(17):7081–7085, 2011.

Cláudia T Codeço. Endemic and epidemic dynamics of cholera: the role of the aquatic reservoir. *BMC Infectious Diseases*, 1(1):1, 2001.

Kashmira A Date, Andrea Vicari, Terri B Hyde, Eric Mintz, M Carolina Danovaro-Holliday, Ariel Henry, Jordan W Tappero, Thierry H Roels, Joseph Abrams, Brenton T Burkholder, et al. Considerations for oral cholera vaccine use during outbreak after earthquake in Haiti, 2010- 2011. *Emerging Infectious Diseases*, 17(11):2105, 2011.

O. Diekmann, JAP Heesterbeek, and MG Roberts. The construction of next-generation matrices for compartmental epidemic models. *Journal of the Royal Society Interface*, 7(47):873–885, 2010.

Odo Diekmann and Johan Andre Peter Heesterbeek. *Mathematical epidemiology of infectious diseases: model building, analysis and interpretation*, volume 5. Wiley, 2000.

Marisa C Eisenberg, Zhisheng Shuai, Joseph H Tien, and P van den Driessche. A cholera model in a patchy environment with water and human movement. *Mathematical Biosciences*, 246(1): 105–112, 2013.

Marino Gatto, Lorenzo Mari, Enrico Bertuzzo, Renato Casagrandi, Lorenzo Righetto, Ignacio Rodriguez-Iturbe, and Andrea Rinaldo. Generalized reproduction numbers and the prediction of patterns in waterborne disease. *Proceedings of the National Academy of Sciences*, 109(48): 19703–19708, 2012.

JM Heffernan, RJ Smith, and LM Wahl. Perspectives on the basic reproductive ratio. *Journal of the Royal Society Interface*, 2(4):281–293, 2005.

Tatsuya Katsumata, Daniel Hosea, Eddy Bagus Wasito, Shigeru Kohno, Kohei Hara, Pitono Soeparto, and Ign Gde Ranuh. Cryptosporidiosis in Indonesia: a hospital-based study and a community-based survey. *The American Journal of Ttropical Medicine and Hygiene*, 59(4):628–632, 1998.

Lorenzo Mari, Enrico Bertuzzo, Lorenzo Righetto, Renato Casagrandi, Marino Gatto, Ignacio Rodriguez-Iturbe, and Andrea Rinaldo. Modelling cholera epidemics: the role of waterways, human mobility and sanitation. *Journal of The Royal Society Interface*, 9(67):376–388, 2012.

Lorenzo Mari, Enrico Bertuzzo, Flavio Finger, Renato Casagrandi, Marino Gatto, and Andrea Rinaldo. On the predictive ability of mechanistic models for the Haitian cholera epidemic. *Journal of The Royal Society Interface*, 12(104):20140840, 2015.

Z. Mukandavire, S. Liao, J. Wang, H. Gaff, D.L. Smith, and J.G. Morris. Estimating the reproductive numbers for the 2008–2009 cholera outbreaks in Zimbabwe. *Proceedings of the National Academy of Sciences*, 108(21):8767–8772, 2011.

Zindoga Mukandavire, David L Smith, and J Glenn Morris Jr. Cholera in Haiti: reproductive numbers and vaccination coverage estimates. *Scientific Reports*, 3, 2013.

A Mwasa and Jean M Tchuenche. Mathematical analysis of a cholera model with public health interventions. *Biosystems*, 105(3):190–200, 2011.

Rachael L Miller Neilan, Elsa Schaefer, Holly Gaff, K Renee Fister, and Suzanne Lenhart. Modeling optimal intervention strategies for cholera. *Bulletin of Mathematical Biology*, 72(8):2004–2018, 2010.

JBH Njagarah and F Nyabadza. A metapopulation model for cholera transmission dynamics between communities linked by migration. *Applied Mathematics and Computation*, 241:317–331, 2014.

Eric K Noji. The public health consequences of disasters. *Prehospital and Disaster Medicine*, 15 (04):21–31, 2000.

Jeffrey M Ochoche. A mathematical model for the transmission dynamics of cholera with control strategy. *International Journal of Science and Technology*, 2(11), 2013.

Renaud Piarroux, Robert Barrais, Benoît Faucher, Rachel Haus, Martine Piarroux, Jean Gaudart, Roc Magloire, Didier Raoult, et al. Understanding the cholera epidemic, Haiti. *Emerging Infectious Diseases*, 17(7):1161, 2011.

Robert B Potter and Sally Lloyd-Evans. *The city in the developing world*. Longman Harlow, 1998.

Andrea Rinaldo, Enrico Bertuzzo, Lorenzo Mari, Lorenzo Righetto, Melanie Blokesch, Marino Gatto, Renato Casagrandi, Megan Murray, Silvan M Vesenbeckh, and Ignacio Rodriguez-Iturbe. Reassessment of the 2010–2011 Haiti cholera outbreak and rainfall-driven multiseason projections. *Proceedings of the National Academy of Sciences*, 109(17):6602–6607, 2012.

Zhisheng Shuai and P van den Driessche. Modelling and control of cholera on networks with a common water source. *Journal of Biological Dynamics*, (ahead-of-print):1–14, 2014.

Zhisheng Shuai, Joseph H Tien, and Pauline van den Driessche. Cholera dynamics on community networks (13rit168) birs research in teams report. 2013.

Ashleigh R. Tuite, Joseph Tien, Marisa Eisenberg, David J.D. Earn, Junling Ma, and David N. Fisman. Cholera epidemic in Haiti, 2010: Using a transmission model to explain spatial spread of disease and identify optimal control interventions. *Annals of Internal Medicine*, 154(9):593–601, 2011. doi: 10.1059/0003-4819-154-9-201105030-00334. URL + `http://dx.doi.org/10.1059/0003-4819-154-9-201105030-00334`.

Albert M Vollaard, Soegianto Ali, Henri AGH van Asten, Suwandhi Widjaja, Leo G Visser, Charles Surjadi, and Jaap T van Dissel. Risk factors for typhoid and paratyphoid fever in jakarta, indonesia. *Jama*, 291(21):2607–2615, 2004.

John T Watson, Michelle Gayer, and Maire A Connolly. Epidemics after natural disasters. *Emerging Infectious Diseases*, 13(1):1, 2007.

WHO. Flooding and communicable diseases fact sheet: Risk assessment and preventive measures. *WHO: Geneva*, 2006.

WHO. Cholera. *http://www.who.int/topics/cholera/en/, accessed August*, 2014.

WHO. Diarrhoeal disease. *http://www.who.int/mediacentre/factsheets/fs330/en/, accessed March*, 2015.

# 3 Figures and Tables

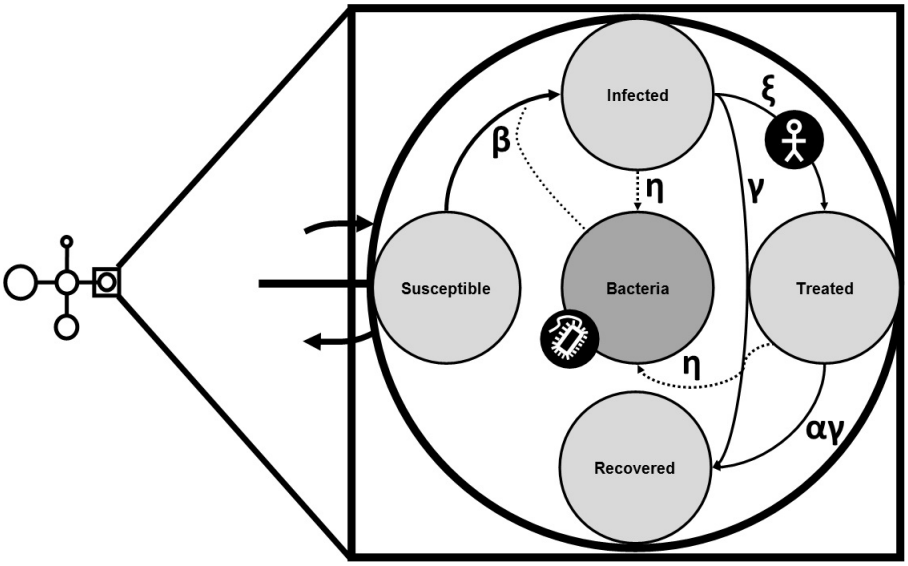



Figure 1: Model structure and interactions. The city, shown on the left, is composed of patches in a star formation. Individuals are resident in a given patch. The peripheral patches are coupled to the central patch by the residents' habitual movement. Peripheral patches are not directly coupled to one another. Resident population density or contact rate with the environment may vary between patches, as denoted by the circle size. Peripheral patches are indexed in ascending order of contact rate or density. In each patch, disease dynamics occur as shown on the right; treatment and decontamination are shown in the black circles.

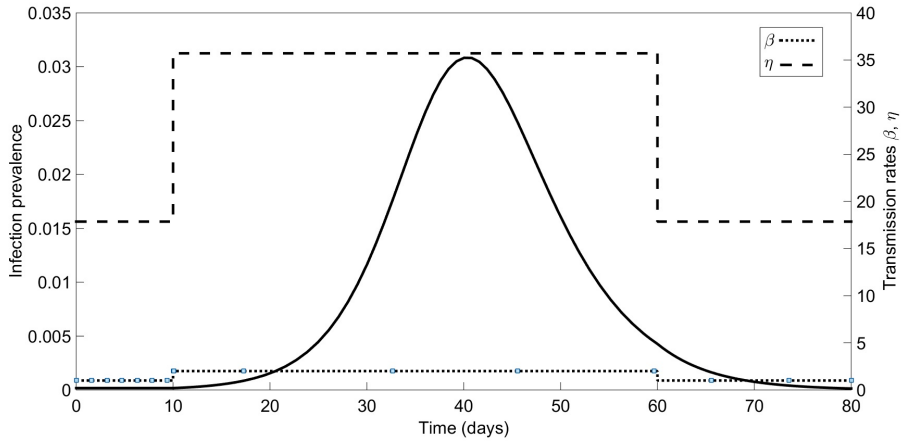



Figure 2: Infection prevalence $\sum_j I_j / \sum_j N_j$ over the course of an epidemic associated with a perturbation to the contact rates $\beta_j$ and shed rate $\eta$ between $t = 10$ an $t = 60$. The system is initially at endemic equilibrium. Parameters values are as in Table 1, with heterogeneous population densities.

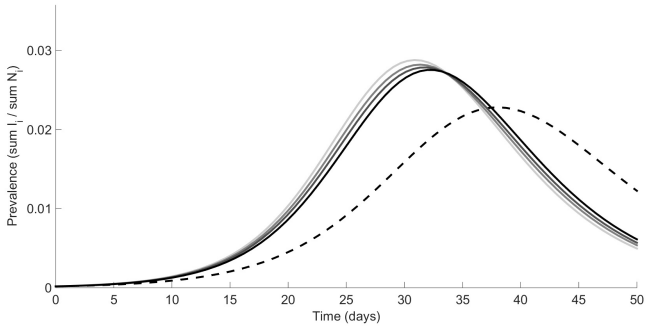



Figure 3: Impact of a single reactively placed decontamination facility on infection prevalence $\sum_j I_j / \sum_j N_j$ following a transmission perturbation at $t = 0$. The decontamination facility was deployed at $t = 0$ in a patch indicated by line type: dashed - centre, solid - peripheral patch $j = 1-4$ with shade indicating the density, black is highest (patch 1). For reference the corresponding epidemic sizes ($\times 10^4$) are 7.91, 8.64, 8.60, 8.57, 8.55 when the decontamination facility is in patch $c, j = 1 - 4$ respectively. Parameter values as in Table 1 with population densities heterogeneous, contact rates homogeneous and disease endemic in the unperturbed system.

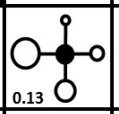
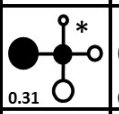
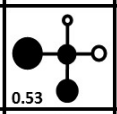
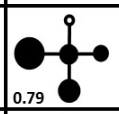
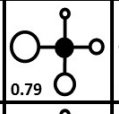
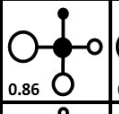
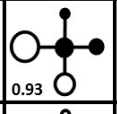
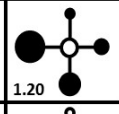
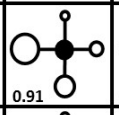
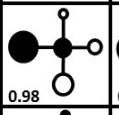
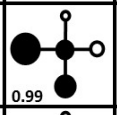
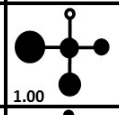
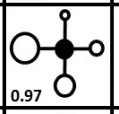
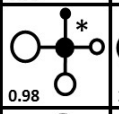
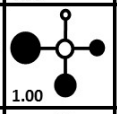
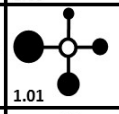
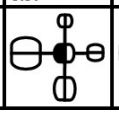
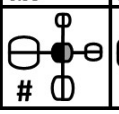
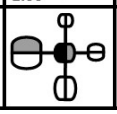
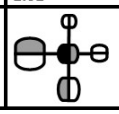
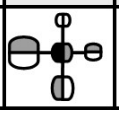
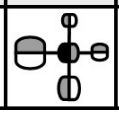
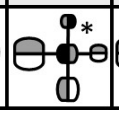
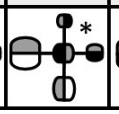
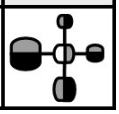
| Equilibrium | Cases | Number of control facilities available | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| Endemic | Decontamination |   |   |   |   | | | | | |
| | Treatment |   |   |   |   | | | | | |
| Disease free | Decontamination |   |   |   |   | | | | | |
| | Treatment |   |   |   |   | | | | | |
| Endemic and Disease free | Decontamination and treatment |  |   |  |  |  |  |   |   |  |

Table 2: Optimal configurations of reactively deployed control facilities to minimize the size of the perturbation-induced epidemic. The top four rows show the configurations of one to four facilities of the same type, decontamination or treatment, in a system that is initially at endemic equilibrium or disease-free equilibrium. The bottom row shows the configurations of one to nine facilities chosen from a pool of five decontamination and five treatment facilities. Configurations are the same for heterogeneous population densities ($N_j$) or environmental contact rates ($\beta_j$). Larger circles indicate patches with higher densities or contact rates. Shaded circles indicate control facility locations. When both types of facility are available, black indicates treatment and grey decontamination. An asterisk (*) denotes that the configuration shown is nearly optimal, but an alternative configuration may be marginally better depending on the heterogeneity. For details see the Supplementary Information Tables S2 and S4. The numerical values indicate, for heterogeneous densities, the impact of the optimal control configurations relative to a full complement of facilities, as quantified by the metric $\delta$, equation (11). Additional values of $\delta$ can be found in the Supplementary Information Table S6. (#) Note that deploying a decontamination and a treatment facility to the central patch reduces $R_0$ below 1 with the perturbed disease-free parameter set. Hence all configurations of two or more facilities that include this dual deployment to the centre prevent an epidemic and are effectively indistinguishable using our method of ranking by epidemic size.

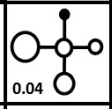
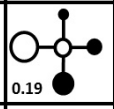
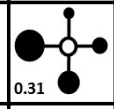
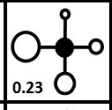
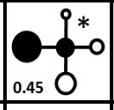
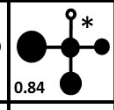
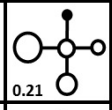
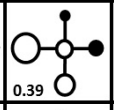
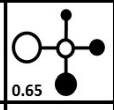
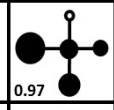
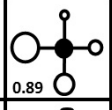
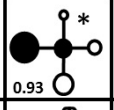
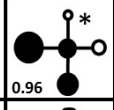
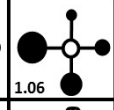
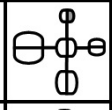
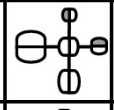
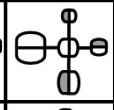
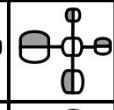
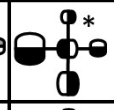
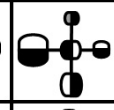
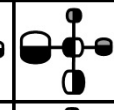
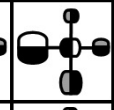
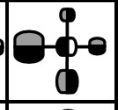
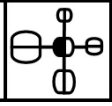
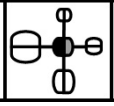
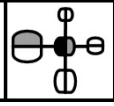
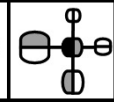
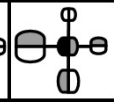
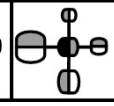
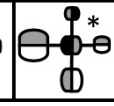
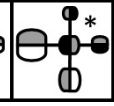
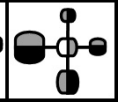
| Cases | Objective | Number of control facilities available | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| Decontamination | Minimise epidemic size |  0.04 |  0.10 |  0.19 |  0.31 | | | | | |
| | Minimise lifetime risk |  0.23 |  * 0.45 |  * 0.65 |  * 0.84 | | | | | |
| Treatment | Minimise epidemic size |  0.21 |  0.39 |  0.65 |  0.97 | | | | | |
| | Minimise lifetime risk |  0.89 |  * 0.93 |  * 0.96 |  1.06 | | | | | |
| Decontamination and treatment | Minimise epidemic size |  |  |  |  |  * |  |  |  |  |
| | Minimise lifetime risk |  |  |  |  |  |  |  * |  * |  |

Table 3: Optimal configurations of pre-emptively deployed control facilities to minimize the lifetime infection risk at endemic equilibrium, or the epidemic size in the event of a perturbation. Configurations are the same for heterogeneous population densities ($N_j$) or environmental contact rates ($\beta_j$). An asterisk (*) denotes that the configuration shown is nearly optimal, but an alternative configuration may be marginally better depending on the heterogeneity. For details see the Supplementary Information Tables S3 and S5. The numerical values indicate, for heterogeneous densities, the impact of the optimal control configurations relative to a full complement of facilities, as quantified by the metric $\delta$. Note that, with regards the epidemic size, under pre-emptive deployment $\delta$ is the increase relative to the uncontrolled epidemic and so is minimised. Additional values of $\delta$ can be found in the Supplementary Information Table S7.

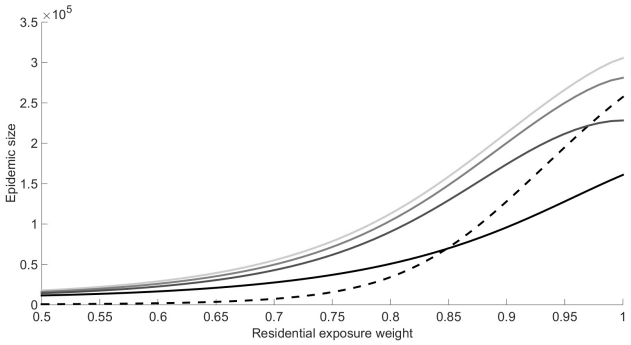



Figure 4: Size of perturbation-induced epidemic depending on the residential exposure weight $\sigma$ when population densities are heterogeneous and the system has one reactively placed decontamination facility. Line style denotes the decontamination facility location: centre (dashed); periphery (solid, darker shades indicate higher densities). The system was initially at disease-free equilibrium. Parameters were as shown in Table 1.

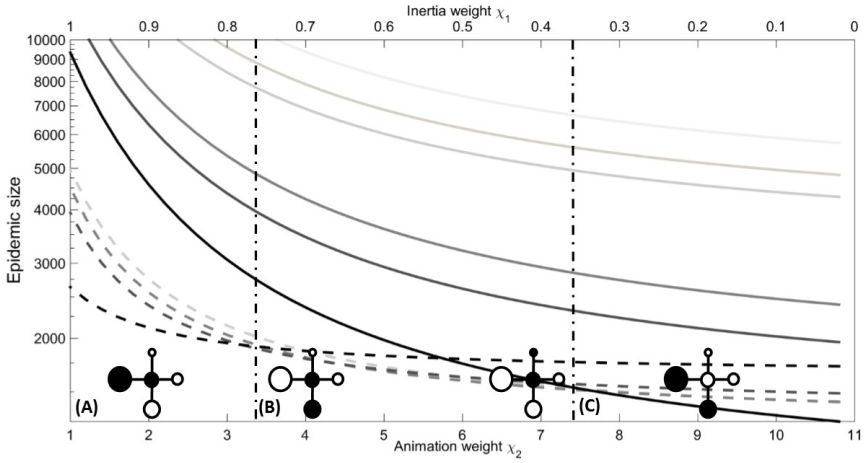



Figure 5: Size of perturbation-induced epidemic depending on the tendency of infected individuals to seek treatment facilities when population densities are heterogeneous and the system has two reactively placed treatment facilities. The tendency to seek treatment is governed by the inertia and animation weights $\chi_1$, $\chi_2$ which, here, are coupled such that $\chi_2 = 1 + 10(1 - \chi_1)$. Line style denotes the treatment facility locations: centre and periphery (dashed, darker shades indicate higher density peripheral patches); periphery only (solid, darker shades indicate higher average densities). In regions A, B and C the optimal configurations are as indicated. Parameters were as in Table 1 with the system initially at disease-free equilibrium.

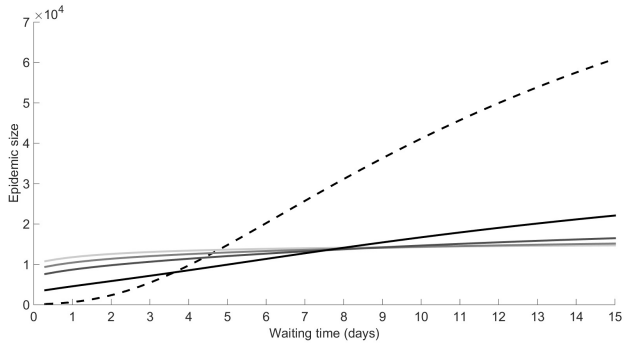



Figure 6: Size of perturbation-induced epidemic depending on the waiting time to treatment $1/\xi$ when population densities are heterogeneous and the system has one reactively placed treatment facility. Line style denotes the treatment facility location: centre (dashed); periphery (solid, darker shades indicate higher densities). The system was initially as disease-free equilibrium. Parameters were as in Table 1.