A stochastic model for MRSA transmission within a hospital ward incorporating environmental contamination

Xing Ju Lee, Glenn R. Fulford, Anthony N. Pettitt and Fabrizio Ruggeri

Supplementary Material

A Additional model details

For all model simulations, the model was initialised with 10 S patients, 5 C_{xd} patients, 5 empty beds and $E(0) = 3.5$. The simulations were ran for 460 days and the simulation of first 100 days were omitted to remove any transient effect of the initial condition. Model inference were made using the latter 360 days (approximately 12 months).

A.1 Parameter estimation for fixed parameters

The ward capacity M and daily admission rate λ were based on the ward from where data used to estimate the individual model force of infection parameters and environmental time series model parameters were collected from [1]. Specifically, the ward capacity was set to 20 (rounded down from 21 in [1]) and λ was set to 5 which achieved a weekly ward occupancy of approximately 94.4% from repeated model simulations (close to the reported rates between 89.7% and 91.8% in [1]). Unfortunately, this data set did not have sufficient information to estimate the other parameters in the model (namely, the probability transitions aside from the probability of being colonised). As such, these parameter estimates were sourced from the literature in similar settings, noting that the data were collected in a UK surgical ward between 2006 and 2007 [1].

The probability of a colonised patient developing an infection used here was originally estimated using ICU data in a UK hospital between 2002 and 2006 [10].

The probabilities of leaving the ward as a susceptible patient (p_L) or colonised patient (q_L) were estimated from the corresponding median length of stay (LOS) durations reported for surgical unit patients in Switzerland between 2004 and 2006 [2]. It was assumed that the p_L and q_L parameters corresponded to the rate parameters of exponential distributions whose medians are as reported in [2] (6 days for susceptible patients and 13 days for patients who were colonised but not infected).

The infection recovery parameter (ψ) was also estimated from the same Swiss data set [2] by fitting the r_C functional form

$$r_C(t|\psi, ti_k) = 1 - \exp\{-\psi(t - ti_k)\}$$

such that $r_C(t) = 0.5$ for when t is equal to the difference in median LOS reported for infected and colonised-only MRSA patients reported in [2], i.e. $r_C(48 - 13|\psi) = 0.5$ where 48 was the median LOS reported for infected patients.

A.2 Parameter estimation for individual model's force of infection

The β parameters were estimated by fitting a non-homogeneous Poisson process (NHPP) to the Dancer et al. [1] data set. The force of infection (FoI) term from NHPP aggregated MRSA-positive patients (T_{xd} and T_d for undetected and detected MRSA-positive patients respectively) as there were insufficient patients to obtain reliable estimates separately for the colonised and infected patients, i.e.

$$FoI_T(t) = \gamma_0 + \gamma_1 T_{xd}(t) + \gamma_2 T_d(t) + \gamma_3 E(t).$$

The γ parameters were estimated using a data-augmented Markov chain Monte Carlo algorithm to impute the unobserved colonisation times (similar to the apporach in [7]). The full details and outputs of the NHPP model are available upon request.

However, the FoI used in the individual model proposed here distinguished between patients with MRSA colonisation from those with an MRSA infection, i.e.

$$FoI_{IM}(t) = \beta_0 + \beta_1 C_{xd}(t) + \beta_2 C_d(t) + \beta_3 I_{xd}(t) + \beta_4 I_d(t) + \beta_5 E(t).$$

In order to use the NHPP parameter estimates to derive estimates for the β terms here, we assume

1. There is a simple relationship between the parameters associated with C and I terms in FoI_{IM}, namely there exists a non-negative parameter ω such that $\beta_3 = \omega\beta_1$ and $\beta_4 = \omega\beta_2$.
2. The background and environmental contamination parameters in FoI_{IM} and FoI_T are identical, i.e. $\beta_0 = \gamma_0$ and $\beta_5 = \gamma_3$.
3. The T terms in FoI_T implicitly averages the 'true' parameters from the C and I patients to arrive at 'homogeneous' γ parameters for the homogeneous MRSA-positive patient cohorts T_{xd} and T_d, e.g. $\gamma_1 T_{xd} = \gamma_1 [(1-p)C_{xd} + (1+p)I_{xd}]$. The parameter p adjusts the 'homogeneous' γ parameter when splitting the T cohort into C and I and is related to the ω parameter in the FoI_{IM} formulation (as shown below).
    - when $p = 0$, the parameters for C and I are the same
    - when $p < 0$, the parameter for C is larger than the corresponding parameter for I
    - when $p > 0$, the parameter for I is larger than the corresponding parameter for C

For the undetected group, we can then relate the FoI components from the two models as follows

$$\gamma_1 [(1-p)C + (1+p)I] = \beta_1 C + \omega\beta_1 I \tag{1}$$

where we have dropped the 'xd' subscripts and time dependence for notational convenience. An identical relationship holds for the detected groups with the appropriate parameters.

To obtain the estimate for β_1 required for the individual model, we solve the simultaneous equation system obtained from matching the coefficients for C and I on the left- and right-hand side of the equality in (1).

$$\begin{aligned} \gamma_1(1-p) = \beta_1 \qquad & \gamma_1(1+p) = \omega\beta_1 \\ & \gamma_1(1+p) = \omega\gamma_1(1-p) \\ & \Rightarrow \omega = \frac{1+p}{1-p} \qquad i.e. \quad p = \frac{\omega-1}{\omega+1}. \end{aligned}$$

Substituting the expression for p back into the expression for β_1,

$$\beta_1 = \gamma_1\left(1 - \frac{\omega-1}{\omega+1}\right) = \gamma_1\frac{2}{\omega+1}$$

such that if $\omega > 1$, then $\beta_1 < \gamma_1$ and $\beta_3 > \gamma_1$ as required from formulation.

A.3 Parameter estimation for time series component

The Dancer et al. [1] data set was also used to fit the time series component of the proposed stochastic model. As the data were originally collected to investigate the effect of a cleaning intervention, the ward received enhanced cleaning for the first half of the study period and normal cleaning for the second half. Of interest here are the estimates associated with the normal cleaning. However given the small number of patients associated with the two time periods, the time series model was fitting using the full data set with the inclusion of an indicator covariate for the intervention $U(t)$ in the ARMAX model where

$$U(t) = \begin{cases} 1 & \text{enchanced cleaning} \\ 0 & \text{normal cleaning.} \end{cases}$$

The other exogenous covariates were the number of undetected colonised and infected patients in the ward. The time a colonised or infected patient is categorised as undetected is assumed to 5 days prior to the day of first positive. The duration of 5 days was the average time between the first positives and first preceding Monday for MRSA patients in the ward (where routine weekly screening would have taken place). This is a simplifying approximation to circumvent the need for data imputation of the undetected duration for all patients on top of the model selection procedure of the appropriate time series model.

The ARMAX(p, q) model for $E(t)$ in this case is then

$$\begin{aligned} & E(t) = \alpha_1 + \alpha_2 C_{xd}(t-1) + \alpha_3 I_{xd}(t-1) + \alpha_4 U(t) + n(t) \\ & (1 - a_1 B - \ldots - a_q B^q)\, n(t) = (1 + b_1 B + ... + b_q B^q)\, z(t) \qquad z(t) \sim WN(0, \sigma^2) \end{aligned}$$

i.e. we assumed that the enhanced cleaning intervention only affected the levels of environmental contamination directly rather than contributions from MRSA patients.

The parameter estimates were obtained using the `auto.arima()` function from the `forecast` package in R. The order selection procedure is a stepwise model selection procedure based on AIC particular to time series models as each model fit is also checked to ensure the fitted model isn't too close to being non-invertible or non-causal [5]. The selected time series model was an ARMAX(2,2) model.

A.4 Additional details on interventions

The five intervention strategies considered in the model investigation are:

1. no colonised on admission (COA) where all patients who are colonised on admission are assumed to be detected on admission and isolated elsewhere, i.e. $\vartheta = 1$ [4].

2. improved environmental cleaning (ENV) which halved the intercept term in the environmental time series model (α_1). [1] found a $32.5\%(95\%\text{CI} : 20.2 - 42.9)$ reduction in mean levels of ward environmental contamination from just the addition of one additional cleaner on weekdays. Therefore, a reduction of 50% should be quite readily achievable from larger scale cleaning interventions which are more typical.

3. improved contact precaution practices (CP) which decreases ν by a factor of ξ where ξ was set to 0.75 based on estimated efficacy of barrier precautions in [6].

4. perfect screening test sensitivity (SENS) where test sensitivity ρ was set to 1 [7].

5. improved decolonisation treatment for colonised patients (DECOL) where the probability for a C_d patient leaving the ward is now $q_L + \Delta$ (with the probability of staying adjusted accordingly). For the simulation results shown, Δ was set to q_L, i.e. colonised patients are twice as likely to leave the ward due to the improved treatment received. In a systematic review on mupirocin (used together with chlorohexadine bathes and throat sprays as decolonisation treatments in [1]) resistance and alternative decolonisation treatment for MRSA [9], it was shown that there was a lack of studies investigating alternative decolonisation options for MRSA despite reports of high levels of mupirocin resistance which could lead to decolonisation failure. As such, the effects of the improvement decolonisation treatment was assumed to be a halving of the expected LOS for colonised patients. Alternative efficacies were also investigated but were not shown to have substantial difference from the chosen value except for alternative values which lead to an increased LOS instead which would unlikely be considered.

A sixth intervention representing improved treatment for infected patients (INF) was initially considered where the infection recovery parameter (ψ) was doubled. This reflected the alternative treatment options to vancomycin to treat MRSA infections such as linezolid (Tsoulas and Nathwani [11] conducted a meta-analysis review on the efficacy of these alternative treatments for MRSA skin and soft-tissue infections). However, direct evidence for the efficacy of alternative treatment options over vancomycin was found to be lacking (and was also shown in an earlier Cochrane review [3] for MRSA surgical site infections). As such, the intervention effect for an infected patient was assumed to be as a result of novel antibacterial treatment which doubles ψ and as such, reduces the period of time an infected patient remains infected notably. While doubling the estimate is potentially overly optimistic, sensitivity analysis on the effect of this intervention (where the intervention effect varied from 0.25 to 3) showed that there was no evident differences in any of the outcome measures when varying the effect size of this intervention singly for both the normal and high burden setting. Thus, this intervention was not considered further here.

The interventions were compared using the generalised Mann-Whitney statistics

$$\theta = Pr(Y > X) + \frac{1}{2}Pr(Y = X)$$

which is approximated by $\hat{\theta} = \frac{U}{mn}$ where

$$U = \sum_{i=1}^{m} \sum_{j=1}^{n} \mathbb{1}(Y_j > X_i) + \frac{1}{2}\mathbb{1}(Y_j = X_i)$$

with $\{Y_j; j = 1, \ldots, n\}$ and $\{X_i; i = 1, \ldots, m\}$ being samples from the Y and X distributions respectively, as defined in the main text.

The confidence intervals for $\hat{\theta}$ were computed based on Method 5 of Newcombe [8]. Specifically, the following equation was solved for θ

$$|\theta - \hat{\theta}| = z\sqrt{\frac{\theta(1-\theta)}{mn}\left[1 + \frac{m_s(1-\theta)}{2-\theta} + \frac{m_s\theta}{1+\theta}\right]}$$

where z is the appropriate standard normal quantile and $m_s = \frac{1}{2}(m+n) - 1$. Both m and n are equal to 1000 for the investigations here. Alternatively, the confidence intervals could be approximated assuming a normal distribution for the test statistic using a central limit theorem argument.

B Parameter sensitivity analysis

To test the sensitivity of the outcome measures to the individual parameters, the simulations were repeated with modified parameter sets. Each modified parameter set had one of the parameters altered from its original value to either a 'high' or 'low' value for that parameter. The high and low values were chosen such that they are symmetric about the mean as specified in Supplementary Table S1.

- low values for the transmission parameters were set to their respective 2.5% quantile estimated previously. The high values were constructed by adding the difference between the low value and mean to the mean.
- the high and low values for the time series parameters were set to be two times the standard error of estimates away from the mean, except for the AR coefficients and noise variance term
  - The high values for the AR coefficients were set to ensure the roots of the AR polynomial are outside the unit circle, i.e. the time series model remains stationary. The low values were then taken to be the mean, less the difference between the mean and high value
  - The high and low values for the noise variance were set to be 1.5 and 0.5 times the mean respectively.

B.1 Normal burden setting

There is little change in the distribution of outcome measures AC, I_{xd} and I_d for both the low and high values of all parameters tested in the normal burden setting.

Parameter	γ_0 ($\times 10^5$)	γ_1 ($\times 10^5$)	γ_2 ($\times 10^5$)	γ_3 ($\times 10^5$)	ω	a_1	a_2	b_1	b_2	α_1	α_2	α_3	σ^2
Low value	11	31.4	1.4	0.1	0.1	1.33	−0.55	0.16	0.18	50	−0.87	0.54	12.25
High value	370	1295	95	5.3	1.9	1.47	−0.41	0.52	0.42	70	0.73	0.66	36.75

Supplementary Table S1: High and low values for the parameters

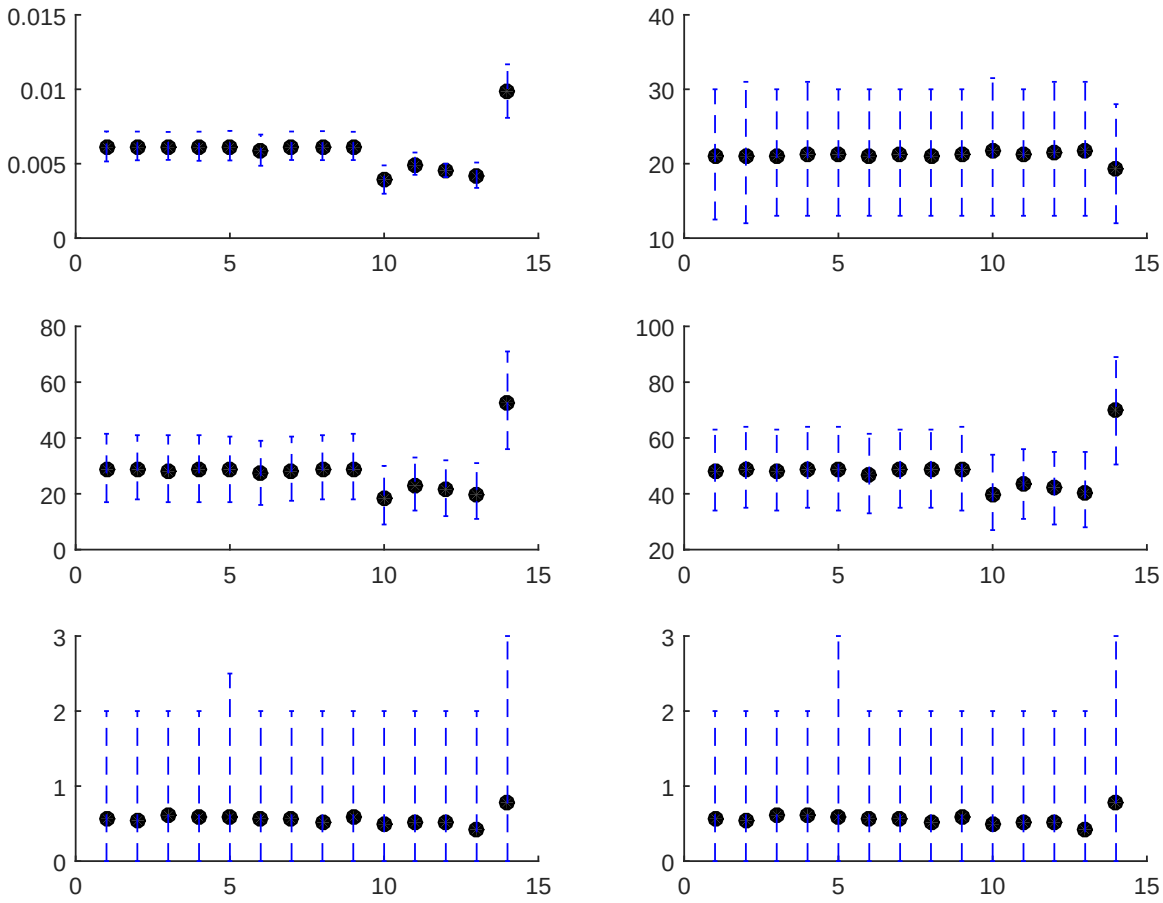
The other three outcomes (AR, C_{xd} and C_d) were most sensitive to changes in the ω parameter, more so for the low ω value tested due to the larger number of colonised patient compared with infected patients in this setting. To a lesser extent, these outcomes were also sensitive to changes in the transmission parameters considered. The outcomes do not appear sensitive to changes in the time series parameters.

There were also notable increases in the spread of the AR outcome associated with the high values tested for a_1 and a_2. These are most likely caused by increasing fluctuations in the time series for $E(t)$ as the parameter values are close to the non-stationary regime for the autoregressive component in the ARMAX model.

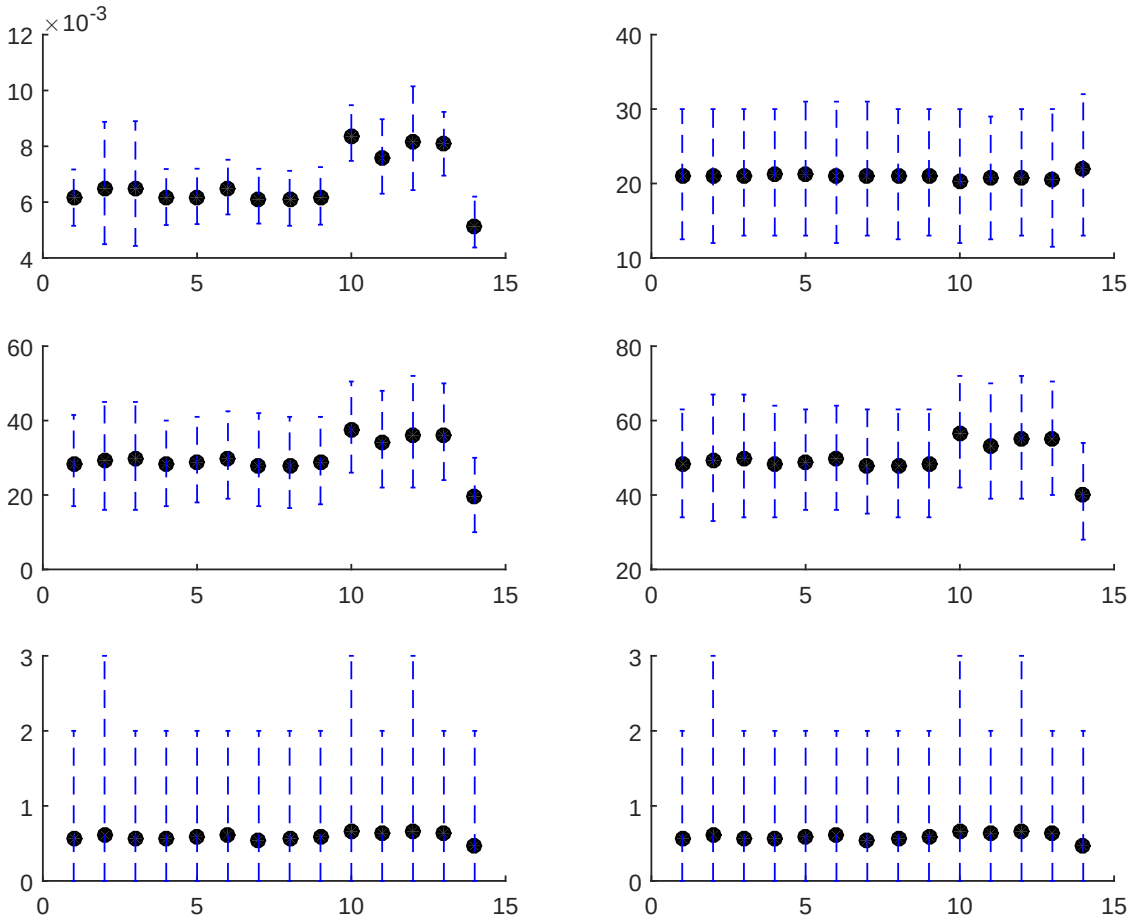
B.2 High burden setting

For the high burden setting, the AC, I_{xd} and I_d outcomes remain relatively insensitive to changes in the parameter values considered. However, there are now slight deviations associated with changes in the ω parameters and the transmission parameters.

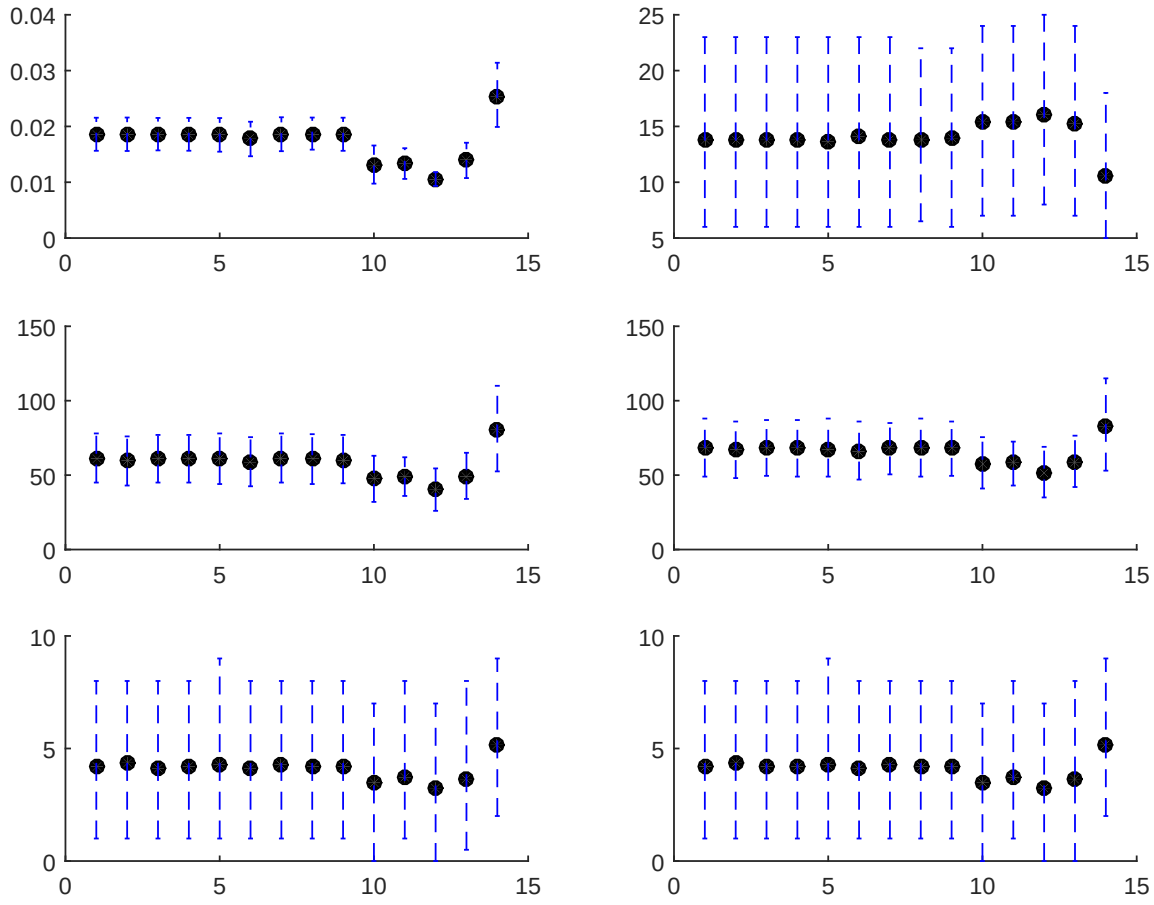
The AR, C_{xd} and C_d outcomes still exhibit notable sensitivity to the changes in the ω parameter value. Changes to the transmission parameters now also notably affect these outcomes, particularly the AR outcome due to the larger number of colonised and infected patients in the high burden setting. These outcomes still appear insensitive to changes in the time series parameters, except for the high a_1 and a_2 parameter values, similar to the normal burden setting.



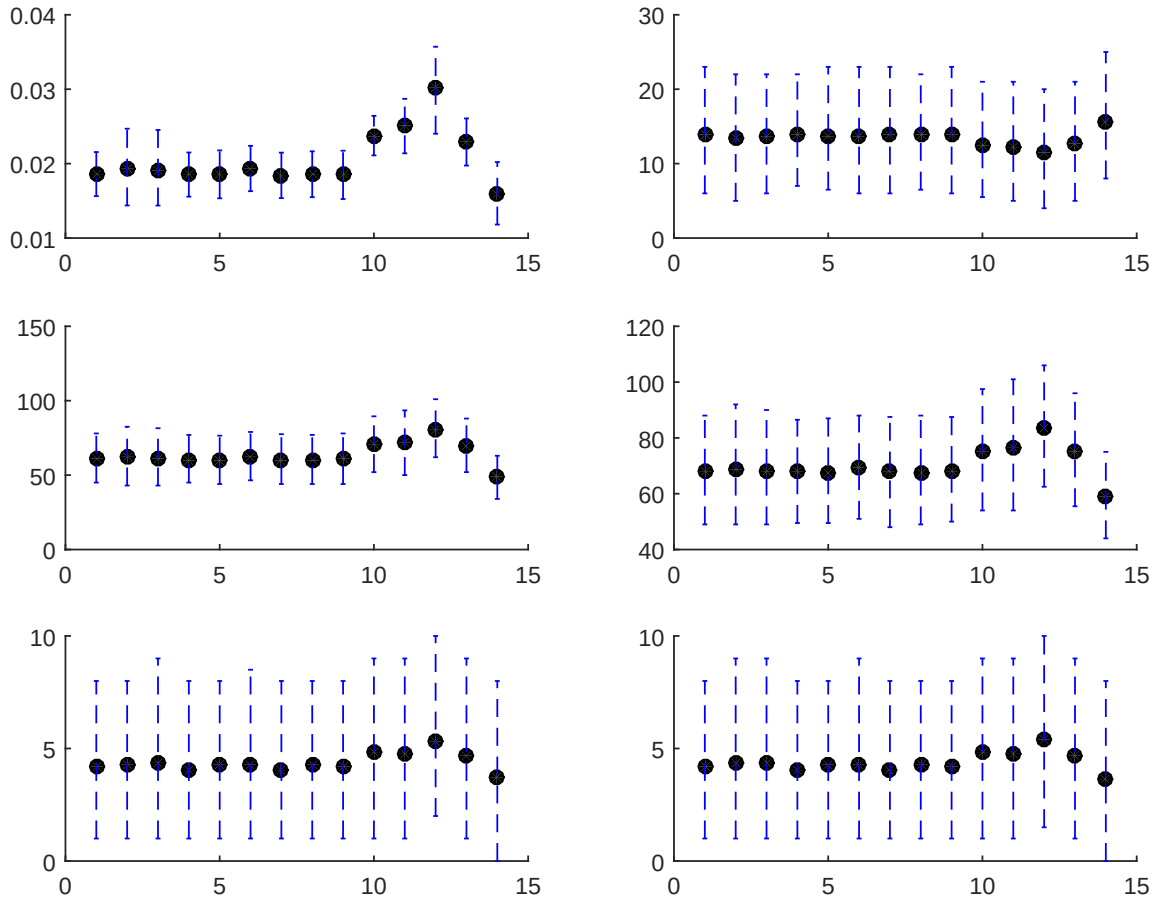
Supplementary Figure S1: Output measures (AR, AC, C_{xd}, C_d, I_{xd}, I_d) for low values of the parameters. The x-axis denotes the different scenarios: baseline, low time series parameters (a_1, a_2,b_1, b_2, α_1,α_2, α_3, σ^2), low transmission parameters (β_0, β_1, β_2, β_5) and low ω.



Supplementary Figure S2: Output measures (AR, AC, C_{xd}, C_d, I_{xd}, I_d) for high values of the parameters. The x-axis denotes the different scenarios: baseline, high time series parameters (a_1, a_2, b_1, b_2, α_1,α_2, α_3, σ^2), high transmission parameters (β_0, β_1, β_2, β_5) and high ω.



Supplementary Figure S3: Output measures (AR, AC, C_{xd}, C_d, I_{xd}, I_d) for low values of the parameters in the high burden setting. The x-axis denotes the different scenarios: baseline, low time series parameters (a_1, a_2,b_1, b_2, α_1,α_2, α_3, σ^2), low transmission parameters (β_0, β_1, β_2, β_5) and low ω.



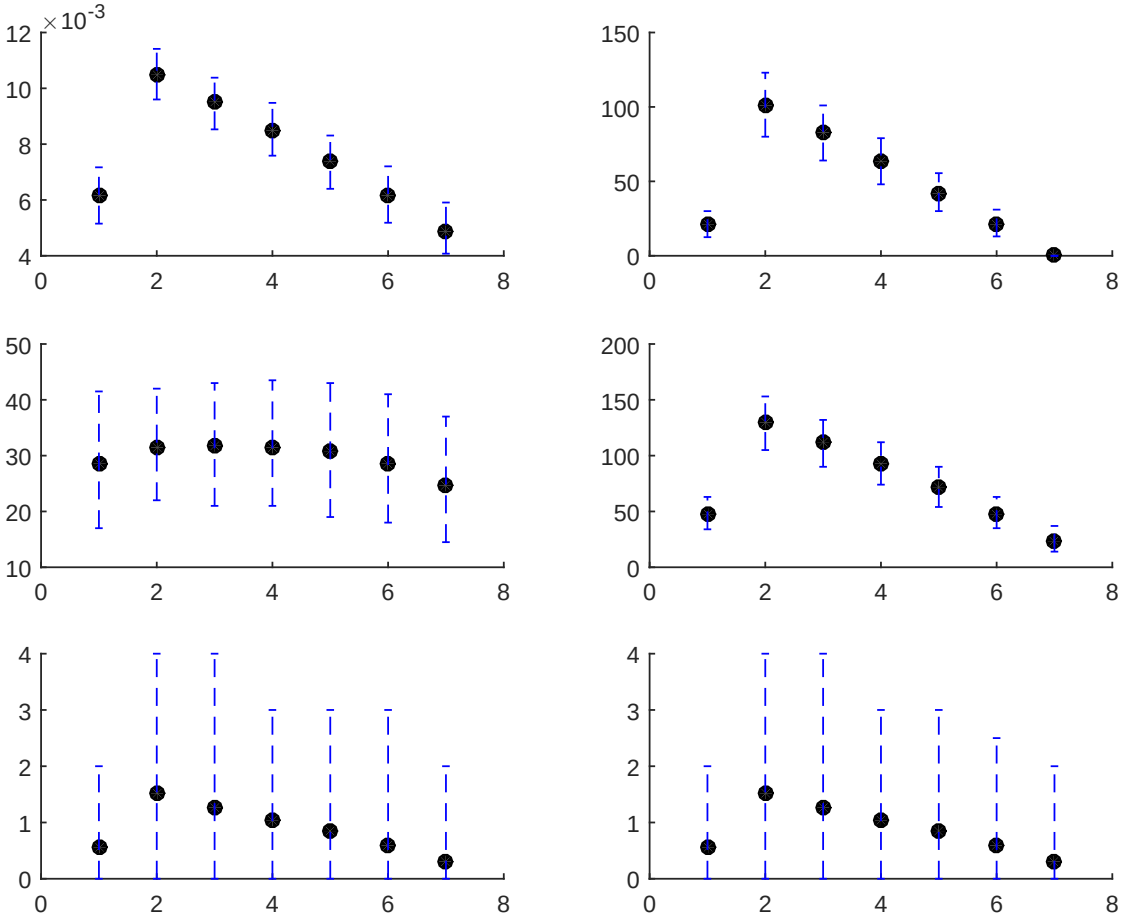
Supplementary Figure S4: Output measures (AR, AC, C_{xd}, C_d, I_{xd}, I_d) for high values of the parameters in the high burden setting. The x-axis denotes the different scenarios: baseline, high time series parameters (a_1, a_2, b_1, b_2, α_1,α_2, α_3, σ^2), high transmission parameters (β_0, β_1, β_2, β_5) and high ω.

C Varying strength of single interventions

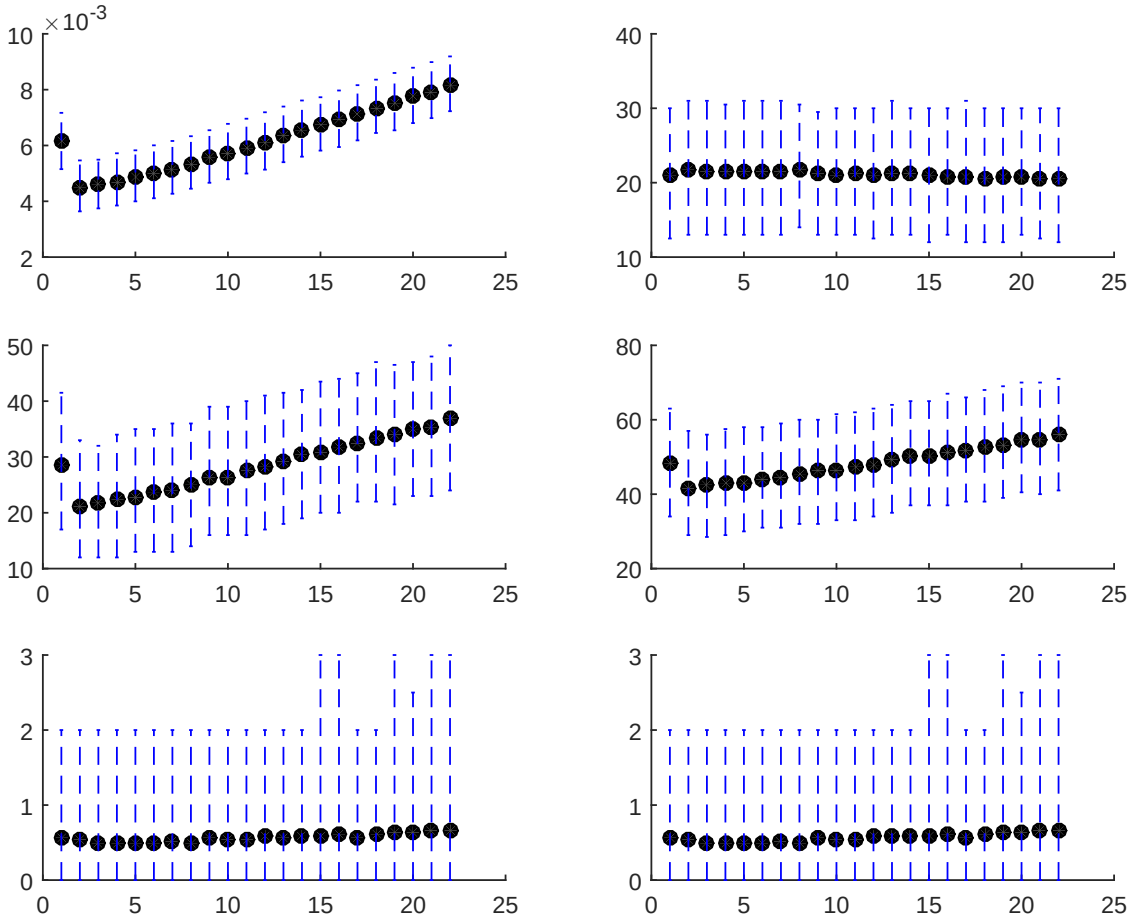
This section presents the six outcome measures (AR, AC, C_{xd}, C_d, I_{xd}, I_d) obtained when varying the magnitude of the six interventions defined in Section A.4 for the normal burden setting (Section C.1) and high burden setting (Section C.2).

There were no notable difference in the infection treatment (INF) intervention (which modifies ψ) across the range of values tested (Supplementary Figure S10 for the normal burden setting and Supplementary Figure S16 for the high burden setting). As such, this intervention was not considered further in the results presented in the main text.

C.1 Normal burden setting

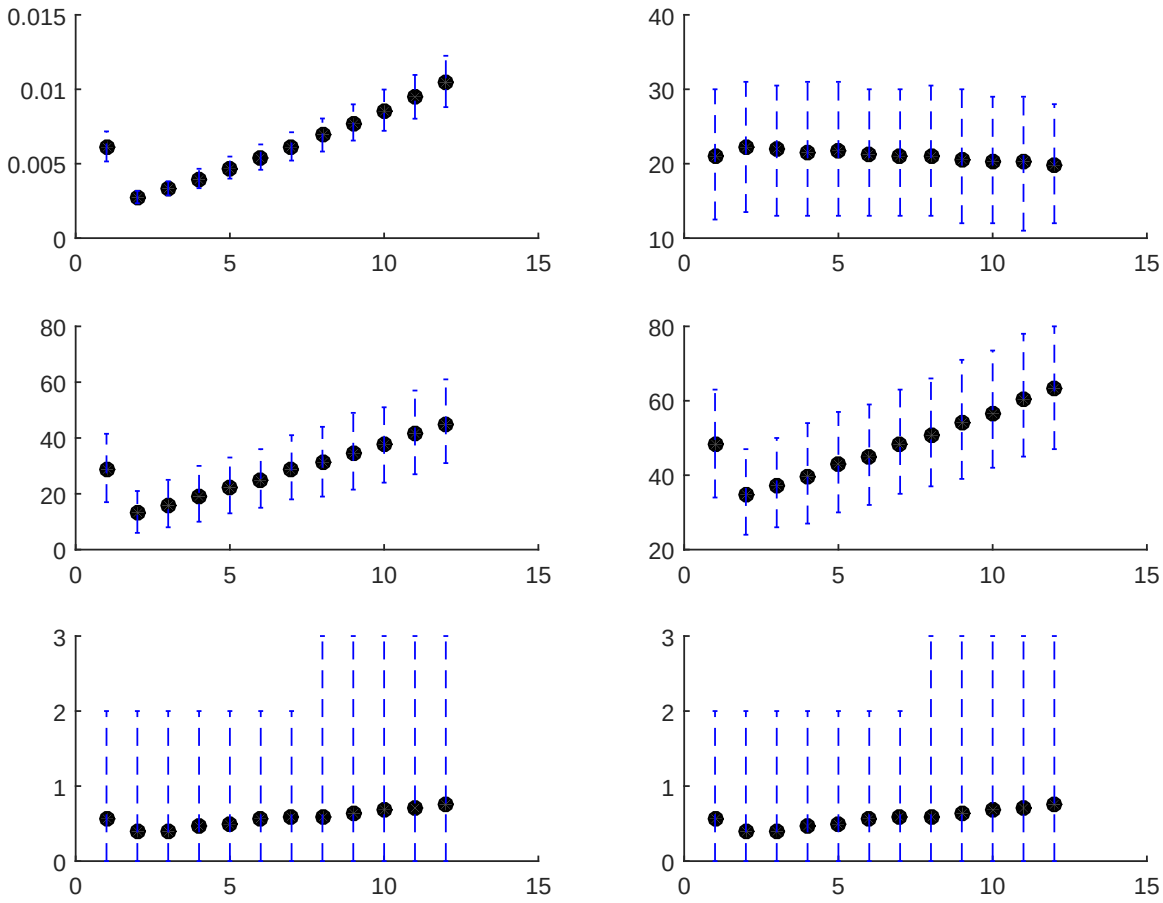


Supplementary Figure S5: Output measures (AR, AC, C_{xd}, C_d, I_{xd}, I_d) for a range of colonised on admission (COA) interventions. The x-axis denotes the different scenarios: baseline, $\vartheta \in \{0.75, 0.8, 0.85, 0.9, 0.95, 1\}$. Baseline value is 0.95.

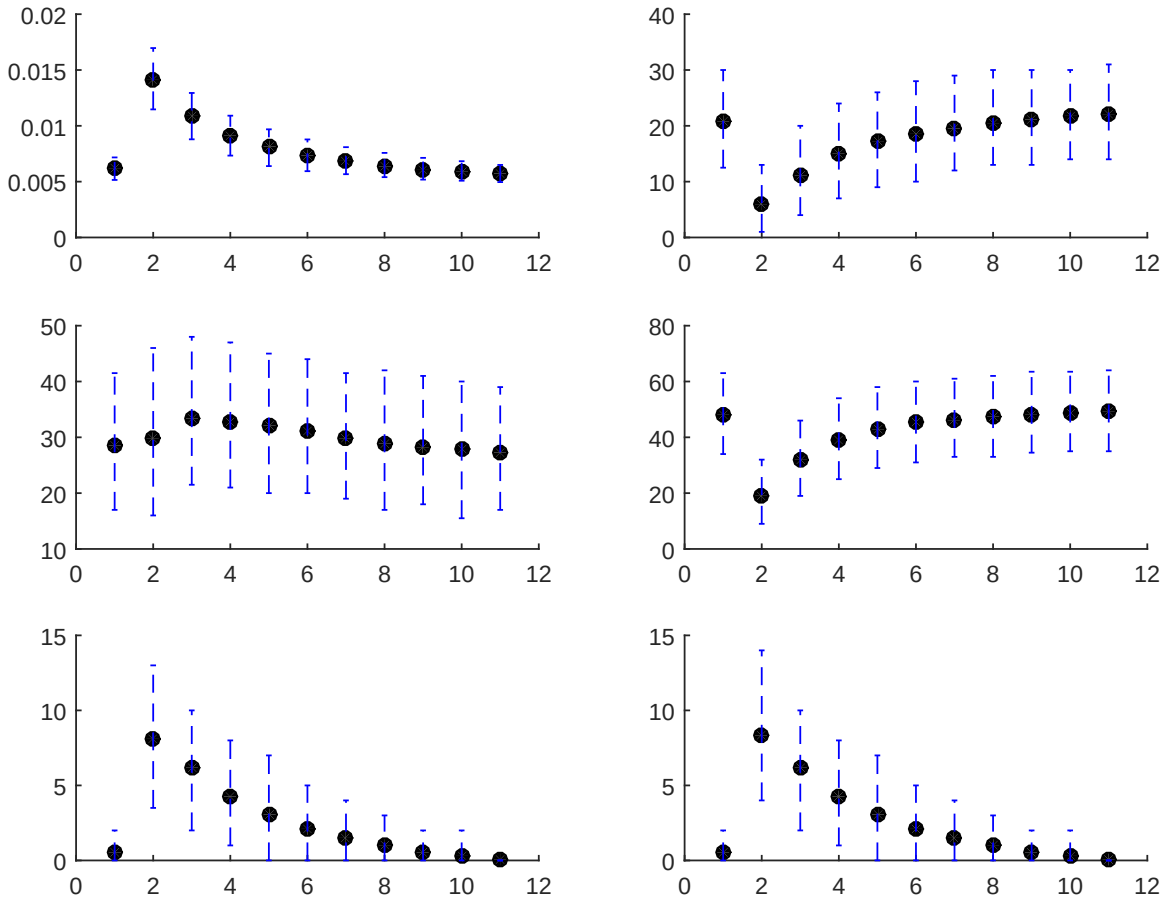


Supplementary Figure S6: Output measures (AR, AC, C_{xd}, C_d, I_{xd}, I_d) for a range of improved environmental contamination (ENV) interventions. The x-axis denotes the different scenarios: baseline, $\alpha_1 \in \{[0, 0.1, \ldots, 2]\alpha_1\}$. Baseline value is α_1.

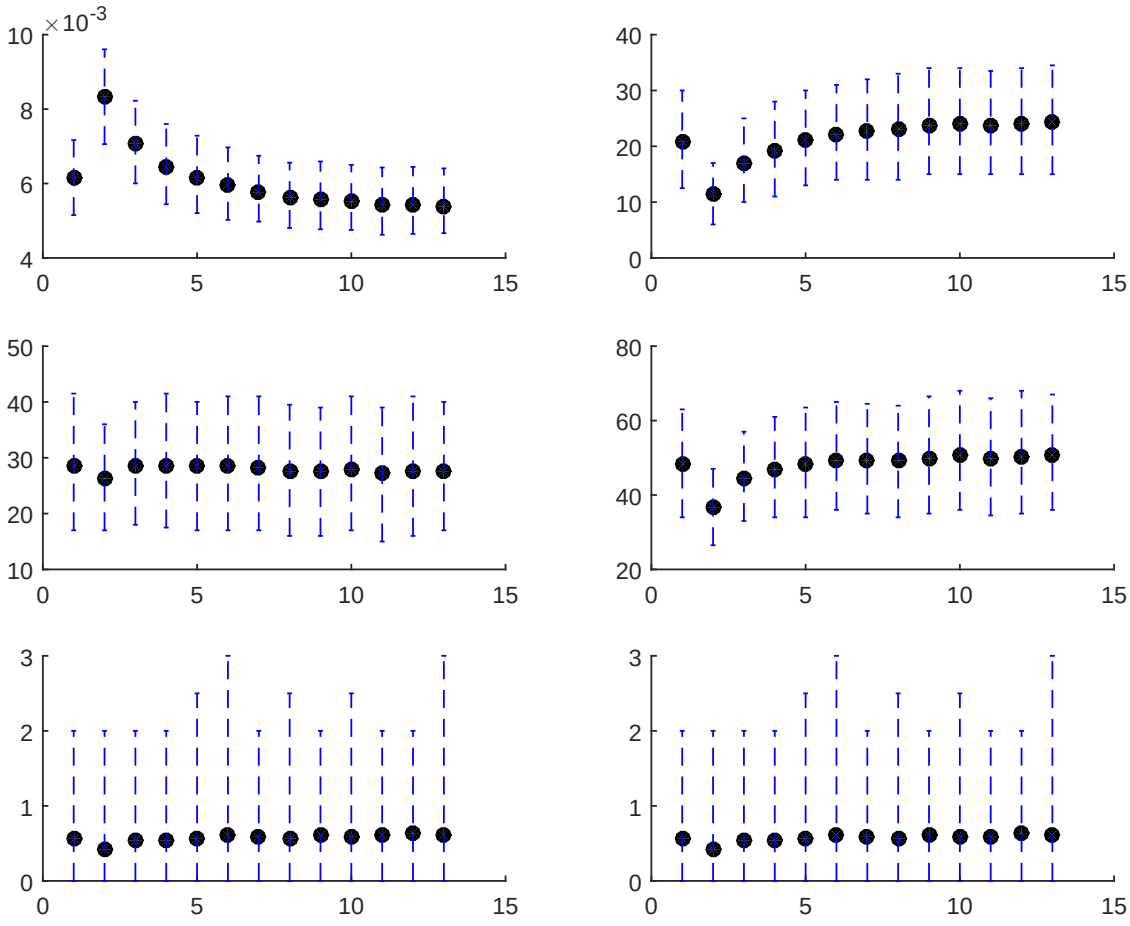
C.2 High burden setting



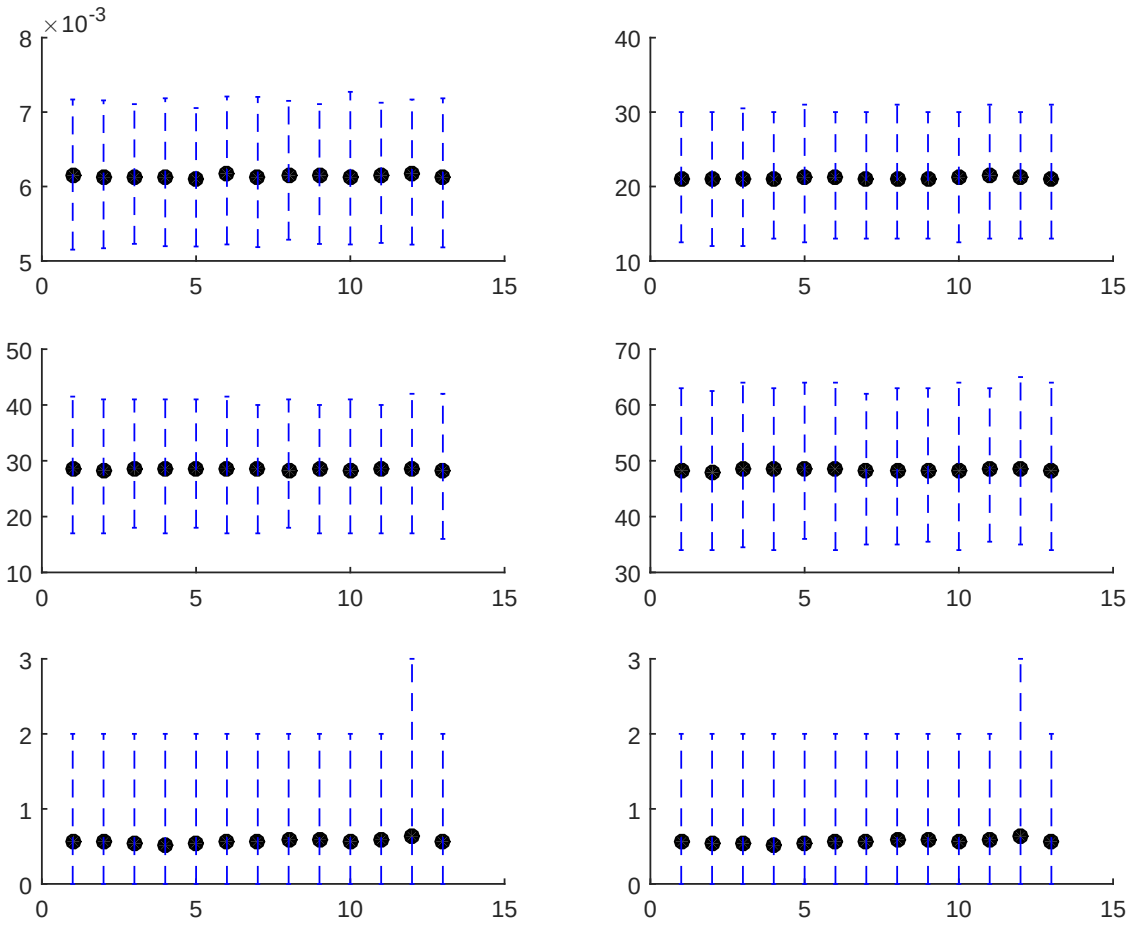
Supplementary Figure S7: Output measures (AR, AC, C_{xd}, C_d, I_{xd}, I_d) for a range of improved contact precaution (CP) interventions. The x-axis denotes the different scenarios: baseline, $\xi \in \{0.5, 0.6, \ldots, 1.5\}$. Baseline value is 1.



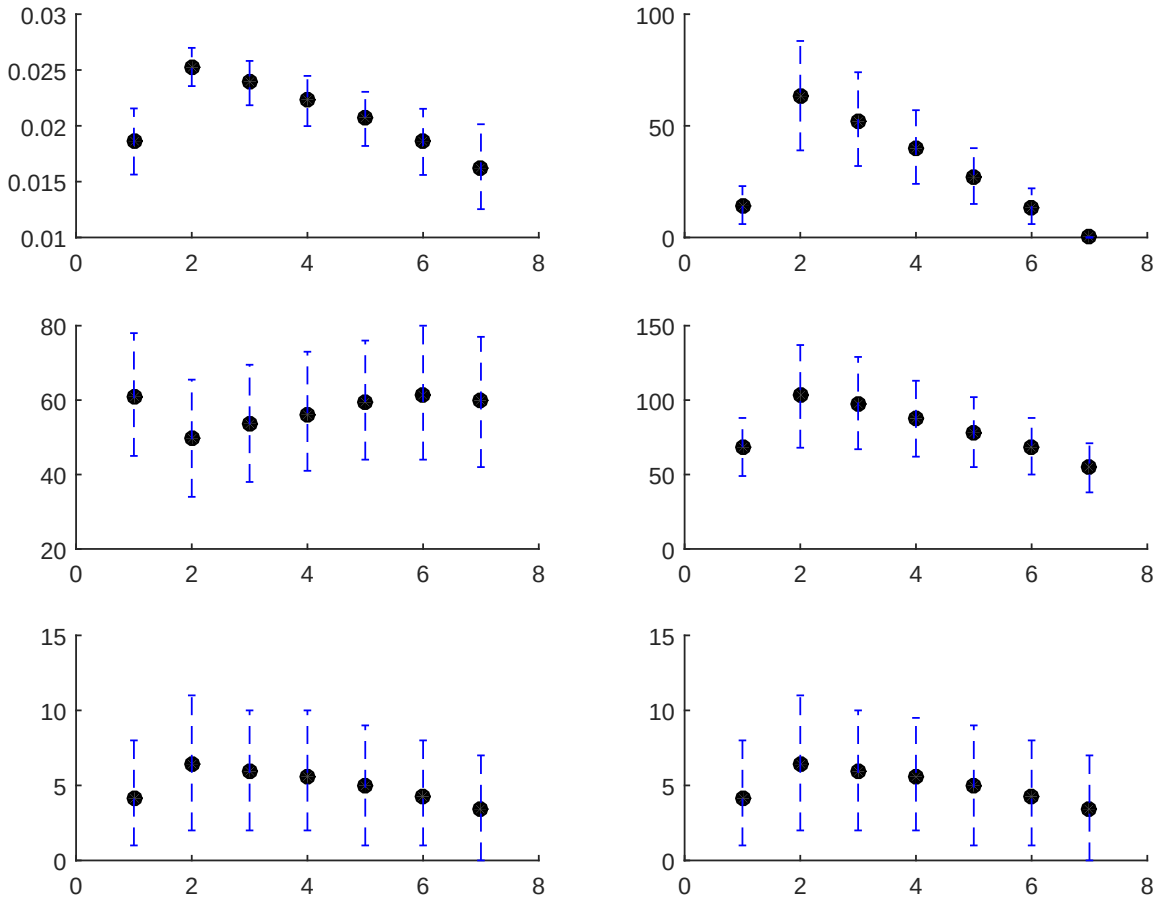
Supplementary Figure S8: Output measures (AR, AC, C_{xd}, C_d, I_{xd}, I_d) for a range of test sensitivity (SENS) interventions. The x-axis denotes the different scenarios: baseline, $\rho \in \{[0.1, 0.2, \ldots, 1\}$. Baseline value is 0.8.



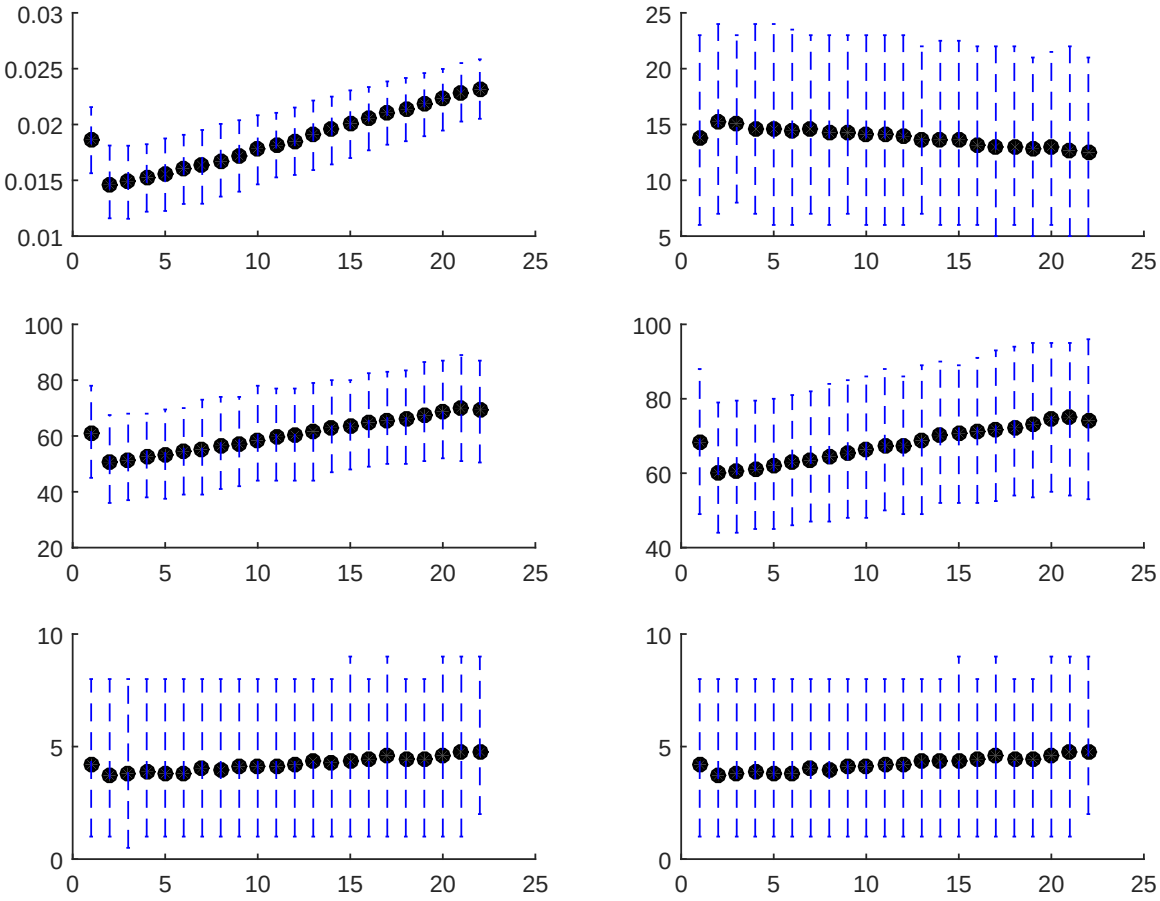
Supplementary Figure S9: Output measures (AR, AC, C_{xd}, C_d, I_{xd}, I_d) for a range of improved decolonisation treatment (DECOL) interventions. The x-axis denotes the different scenarios: baseline, $\Delta \in \{[-0.75, -0.5, \ldots, 2]q_L\}$. Baseline value is 0.



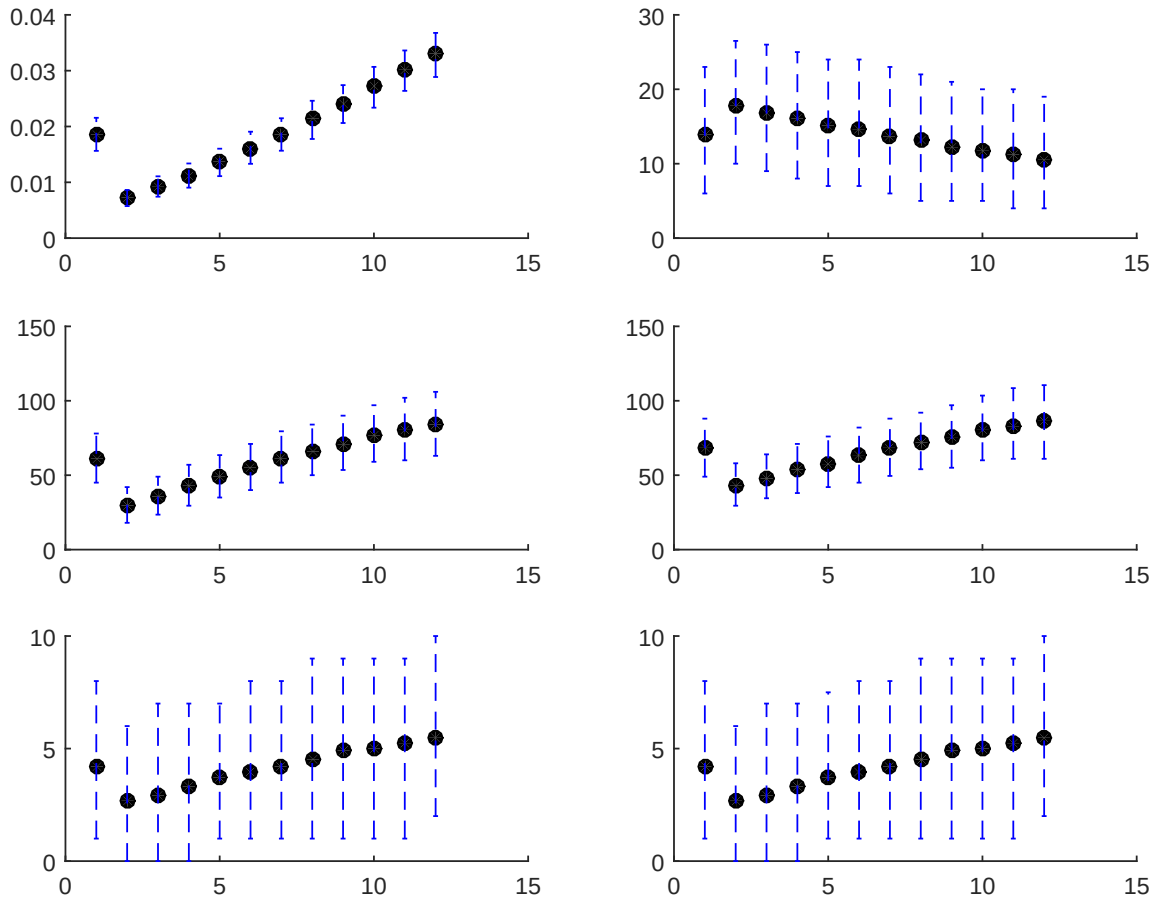
Supplementary Figure S10: Output measures (AR, AC, C_{xd}, C_d, I_{xd}, I_d) for a range of improved infection treatment (INF) interventions. The x-axis denotes the different scenarios: baseline, $\psi \in \{[0.25, 0.5, \ldots, 3]\psi\}$. Baseline value is ψ.



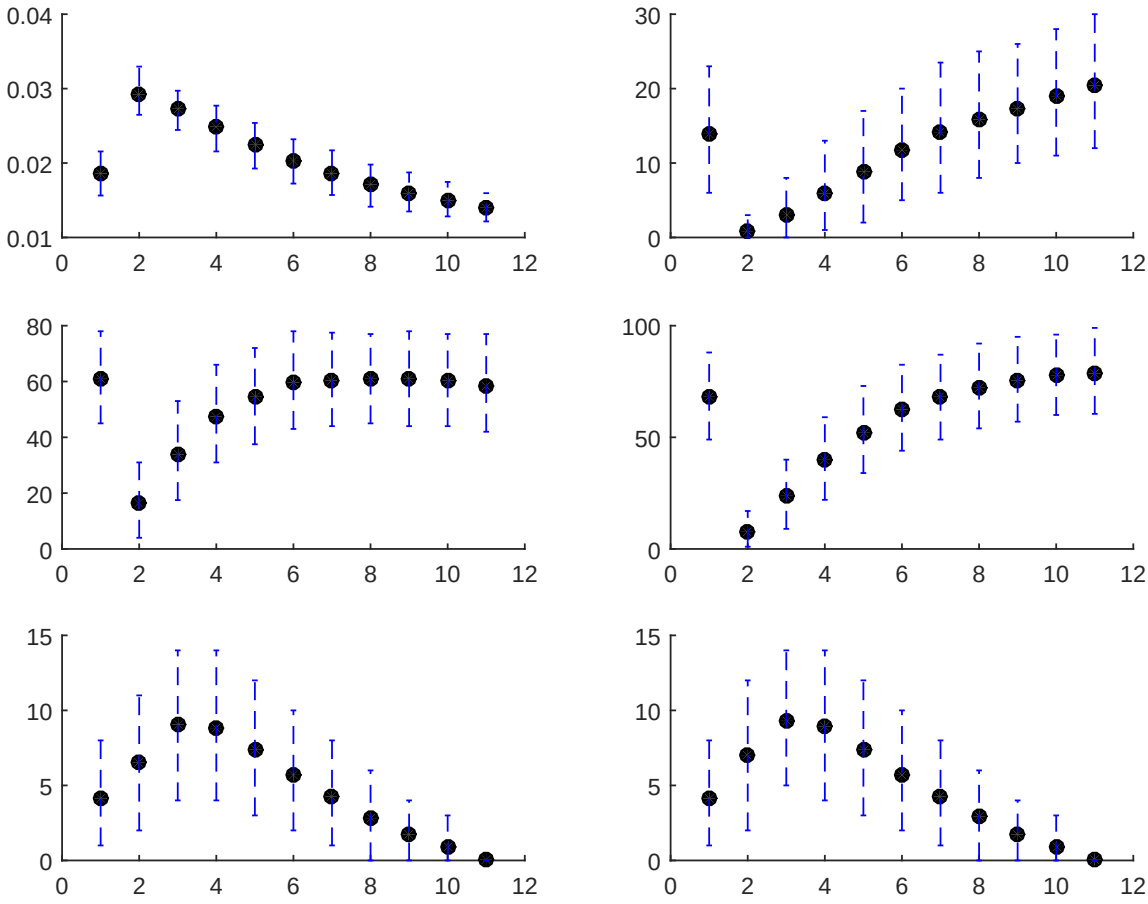
Supplementary Figure S11: Output measures (AR, AC, C_{xd}, C_d, I_{xd}, I_d) for a range of colonised on admission (COA) interventions in the high burden setting. The x-axis denotes the different scenarios: baseline, $\vartheta \in \{0.75, 0.8, 0.85, 0.9, 0.95, 1\}$. Baseline value is 0.95.



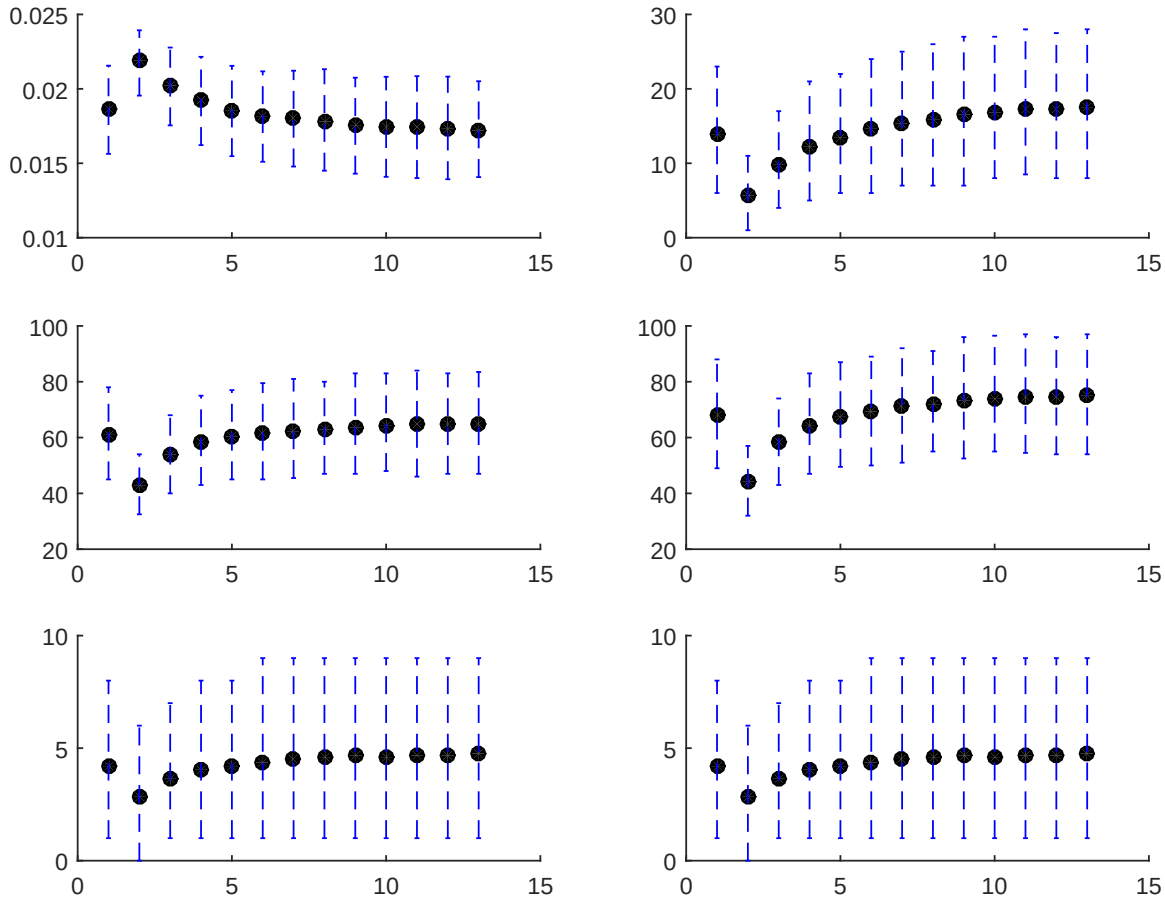
Supplementary Figure S12: Output measures (AR, AC, C_{xd}, C_d, I_{xd}, I_d) for a range of improved environmental contamination (ENV) interventions in the high burden setting. The x-axis denotes the different scenarios: baseline, $\alpha_1 \in \{[0, 0.1, \ldots, 2]\alpha_1\}$. Baseline value is α_1.



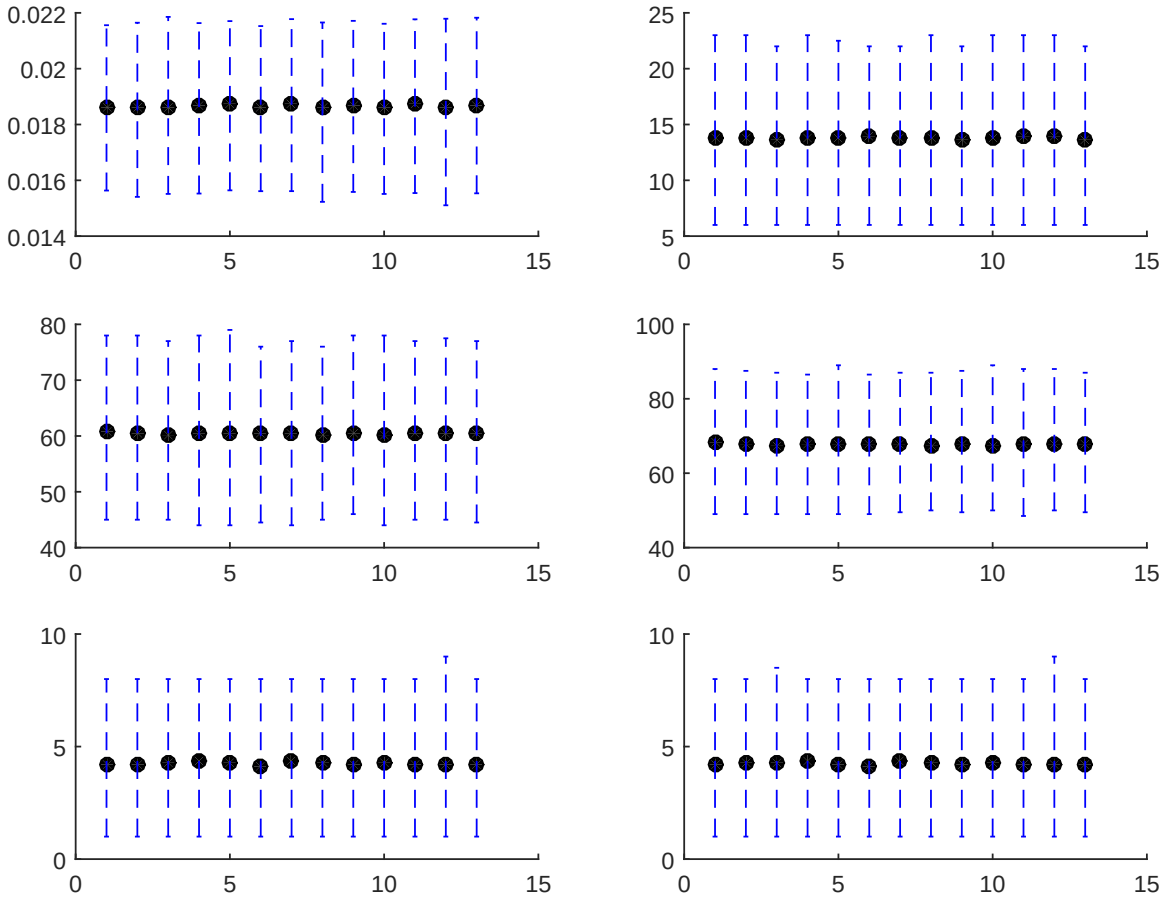
Supplementary Figure S13: Output measures (AR, AC, C_{xd}, C_d, I_{xd}, I_d) for a range of improved contact precaution (CP) interventions in the high burden setting. The x-axis denotes the different scenarios: baseline, $\xi \in \{0.5, 0.6, \ldots, 1.5\}$. Baseline value is 1.



Supplementary Figure S14: Output measures (AR, AC, C_{xd}, C_d, I_{xd}, I_d) for a range of test sensitivity (SENS) interventions in the high burden setting. The x-axis denotes the different scenarios: baseline, $\rho \in \{[0.1, 0.2, \ldots, 1\}$. Baseline value is 0.8.



Supplementary Figure S15: Output measures (AR, AC, C_{xd}, C_d, I_{xd}, I_d) for a range of improved decolonisation treatment (DECOL) interventions in the high burden setting. The x-axis denotes the different scenarios: baseline, $\Delta \in \{[-0.75, -0.5, \ldots, 2]q_L\}$. Baseline value is 0.



Supplementary Figure S16: Output measures (AR, AC, C_{xd}, C_d, I_{xd}, I_d) for a range of improved infection treatment (INF) interventions in the high burden setting. The x-axis denotes the different scenarios: baseline, $\psi \in \{[0.25, 0.5, \ldots, 3]\psi\}$. Baseline value is ψ.

D Additional results for normal burden setting

The plots of the average and 95% intervals of the different outcome measures (Supplementary Figures S17, S18, S19, S20, S21 and S22) share the same x-axis label ordering which denotes the different intervention combinations. The x-axis label ordering, moving from left to right, is

- the baseline scenario,
- single interventions (COA, ENV, CP, SENS, DECOL),
- two interventions ({COA, ENV}, {COA, CP}, {COA, SENS}, {COA, DECOL}, {ENV, CP}, {ENV, SENS}, {ENV, DECOL}, {CP, SENS}, {CP, DECOL}, and {SENS, DECOL}),
- three interventions ({COA, ENV, CP}, {COA, ENV, SENS}, {COA, ENV, DECOL}, {COA, CP, SENS}, {COA, CP, DECOL}, {COA, SENS, DECOL}, {ENV, CP, SENS}, {ENV, CP, DECOL}, {ENV, SENS, DECOL}, and {CP, SENS, DECOL}),
- four interventions ({COA, ENV, CP, SENS}, {COA, ENV, CP, DECOL}, {COA, ENV, SENS, DECOL}, {COA, CP, SENS, DECOL} and {ENV, CP, SENS, DECOL}), and
- all five interventions combined.

The same ordering is also used in the corresponding plots for the high burden setting (Supplementary Figures S23, S24, S25, S26, S27 and S28).

D.1 AR outcome

All single interventions decreased the AR outcome measure, with the largest improvement obtained for the CP intervention out of all five interventions singly. The CP intervention also produced an AR distribution which is distributionally smaller than the other single interventions. This result was perhaps unsurprising as the CP intervention directly affects the AR outcome measure.

The best performing intervention pair in reducing the AR outcome was the {COA, CP} pair. While there was only weak evidence that the AR distribution associated with this pair was smaller than that of the second best performing pair ({ENV, CP} with $\hat{\theta} = 0.25(0.23, 0.27)$), it was substantially smaller than the AR distributions of the next three best performing intervention pairs ({COA, ENV}, {CP, DECOL} and {CP, SENS}).

The best performing intervention triplet was {COA, ENV, CP} which had an AR distribution substantially smaller than the other nine triplets. θ estimates for the comparison of {COA, ENV, CP} with the four next best performing intervention triplets are provided in Supplementary Table S3.

The best performing intervention quartet in terms of the AR outcome was {COA, ENV, CP, DECOL}. However, its associated AR distribution is similar to that of the {COA, ENV, CP, SENS} with an estimated θ value of $0.43(0.41, 0.46)$. While the mean AR estimate for {COA, ENV, CP, DECOL} was smaller than that for {COA, ENV, CP, SENS}, the latter had a narrower 95% interval

compared with the former. These two quartets performed better than the remaining three quartets.

Comparing across the best performing intervention combinations for the AR outcome, the {COA, CP} pair outperforms CP singly and {COA, ENV, CP} triplet outperforms the {COA, CP} pair. However, the reductions in the AR distribution moving from the best performing triplet to either of the two best performing quartets ({COA, ENV, CP, DECOL} or {COA, ENV, CP, SENS}) are less pronounced (with associated $\hat{\theta}$ of $0.33(0.30, 0.35)$ and $0.38(0.35, 0.40)$ respectively). The AR distribution for the case with all interventions was slightly smaller compared with the best performing triplet ({COA, ENV, CP}) with an estimated θ of $0.20(0.18, 0.22)$ and a narrower 95% interval. While the case with all interventions also outperformed the two best performing intervention quartets, the difference in the AR distributions here was less pronounced compared with the triplet comparison with $\hat{\theta}$ of $0.35(0.33, 0.38)$ and $0.28(0.26, 0.30)$ for the best and second best performing intervention quartets respectively.

D.2 AC outcome

The most important intervention for the AC outcome was obviously the COA intervention which eliminates the possibility of colonised patients being admitted. As such, the COA intervention (and any other intervention combinations which include COA) greatly outperforms interventions of any size which do not include the COA intervention.

D.3 C_{xd} outcome

In terms of the C_{xd} outcome distribution, the most effective single intervention appears to be the CP intervention with an estimated θ value of $0.17(0.15, 0.19)$. The COA and ENV interventions performed similarly to one another and produced a slightly smaller C_{xd} distribution compared with the baseline. The SENS and DECOL interventions singly did not seem to have affected the C_{xd} distribution when compared with the baseline. As such, the CP intervention outperforms the COA and ENV interventions and is superior to that of SENS and DECOL interventions in producing a smaller C_{xd} distribution.

The most effective intervention pair in reducing the C_{xd} outcome average was the {COA, CP} pair. However, the second best pairing {ENV, CP} produced a similar outcome distribution ($\hat{\theta} = 0.50(0.47, 0.52)$). More notable reduction in the C_{xd} distributions were observed when comparing {COA, CP} to subsequent best performing pairs.

The {COA, ENV, CP} triplet was the most effective triplet in producing a smaller C_{xd} distribution, slightly outperforming the next four most effective triplets with $\hat{\theta}$ values of 0.35 or 0.32. Improved performance was noted when comparing the {COA, ENV, CP} triplet with subsequent triplets.

The most effective quartet of interventions appear to be either {COA, ENV, CP, DECOL} or {COA, ENV, CP, SENS} with similar distributions ($\hat{\theta} = 0.48(0.46, 0.51)$). Both these intervention quartets performed better than the other three quartets considered for the C_{xd} outcome.

Comparing across the different intervention combination sizes, the two best performing pairs ({COA, CP} and {ENV, CP}) performed slightly better in reducing the C_{xd} distribution

compared with CP singly. A similar performance gain was noted when comparing the best intervention triplet ({COA, ENV, CP}) to both the best performing pairs. There does not appear to be substantial difference in the C_{xd} difference when comparing across the best performing triplet, quartets and the combination of all interventions.

D.4 C_d outcome

Of the five single interventions, only the COA, ENV and CP interventions produced a smaller C_d distributional outcome. The SENS and DECOL interventions did not produce C_d distributions that were notably different from baseline. The best performing single intervention in terms of the C_d outcome measure was the COA intervention, which greatly outperformed all four other single interventions.

The importance of the COA intervention for the C_d outcome measure was also reflected in the drastically smaller C_d distributions obtained for interventions sets with COA included compared with those without the COA intervention included.

The best performing intervention pair for the C_d outcome was {COA, CP}. The associated C_d distribution for {COA, CP} was slightly smaller compared with the second best pair ({COA, ENV} with $\hat{\theta}$ of $0.38(0.35, 0.40)$). Improved performance was noted when comparing {COA, CP} with the three next best performing intervention pairs for the C_d outcome ({COA, DECOL}, {COA, SENS}, and {ENV, CP} with θ values of $0.19(0.17, 0.21)$, $0.18(0.16, 0.20)$ and $0.00(0.00, 0.01)$ respectively).

The best performing triplet was {COA, ENV, CP} with slight evidence that the associated C_d distribution was smaller than those of the next four best performing triplets with $\hat{\theta}$ estimates between 0.24 and 0.33. There was stronger evidence that the {COA, ENV, CP} triplet outperformed the next {COA, SENS, DECOL} triplet (the sixth best performing triplet) with $\hat{\theta}$ of $0.10(0.08, 0.11)$.

The two best performing quartets were {COA, ENV, CP, DECOL} and {COA, ENV, CP, SENS}, outperforming the other three quartets, in particular the quartet without the COA intervention.

Comparing across different intervention sizes, the are notable reductions in support of considering additional number of interventions up to the best performing intervention triplet ({COA, ENV, CP}) for the C_d outcome. There are no discernible difference in the C_d outcome distributions in implementing all five interventions or either of the two best performing quartets identified compared with having just the best performing intervention triplet (with θ estimates ranging from 0.46 to 0.51).

D.5 I_{xd} outcome

The SENS intervention was the most effective intervention for the I_{xd} outcome measure as having perfect sensitivity in the screening test ensures detection of colonised patients prior to the colonisation developing into an infection. As such, the SENS intervention singly was sufficient to reduce the I_{xd} outcome to 0. Any other intervention combinations with SENS was also able to achieve the same outcome for I_{xd}. However, it should also be noted that the I_{xd} outcome is generally small for the particular ward setting considered with even the

baseline I_{xd} having a 95% interval of $[0, 2]$ (see Supplementary Figure S21).

There appears to be little difference in the I_{xd} outcome of the other single interventions (apart from SENS with $\hat{\theta} = 0.28(0.26, 0.30)$) compared with the baseline distribution with θ estimates ranging from 0.39 to 0.51. The SENS intervention only slightly outperform the other single interventions with $\hat{\theta}$ values ranging from 0.28 to 0.38 when compared with the other four single interventions. There is little evidence that the second best intervention (COA) is different from the remaining three single interventions (CP, ENV, DECOL) with $\hat{\theta}$ between 0.39 to 0.42.

With the combinations of two interventions, we see that any intervention pairs including SENS would achieve I_{xd} of 0. Thus, the comparison of the intervention pairs which exclude SENS was done with a representative intervention pair {SENS, .} denoting an intervention pair including SENS (as there is no need to compare between intervention pairs including SENS). Similarly, denoting any intervention triplet which include SENS by {SENS, ., .} and any intervention quartet with SENS by {SENS, ., ., .} , the eradication of I_{xd} only slightly outperforms the other interventions of similar sizes with $\hat{\theta}$ ranging between 0.28 to 0.43. This marginal gain is, again, due to the small numbers of I_{xd} involved.

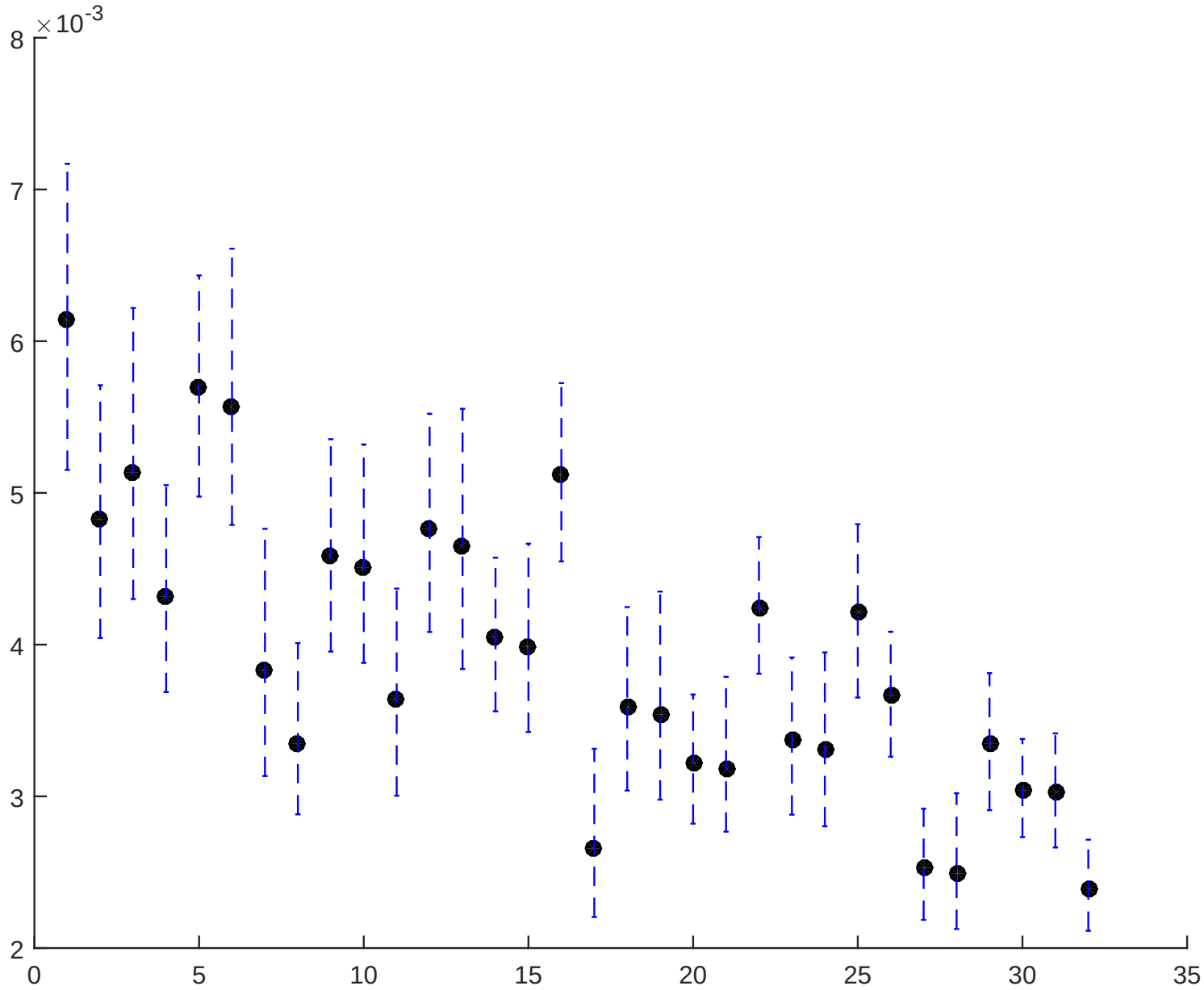
Lastly, comparing across the different intervention sizes including SENS, it is unsurprising that there is no difference between their I_{xd} distributions. In other words, if the focus was solely on minimising I_{xd}, there is no need to consider anything beyond the SENS intervention singly.

D.6 I_d outcome

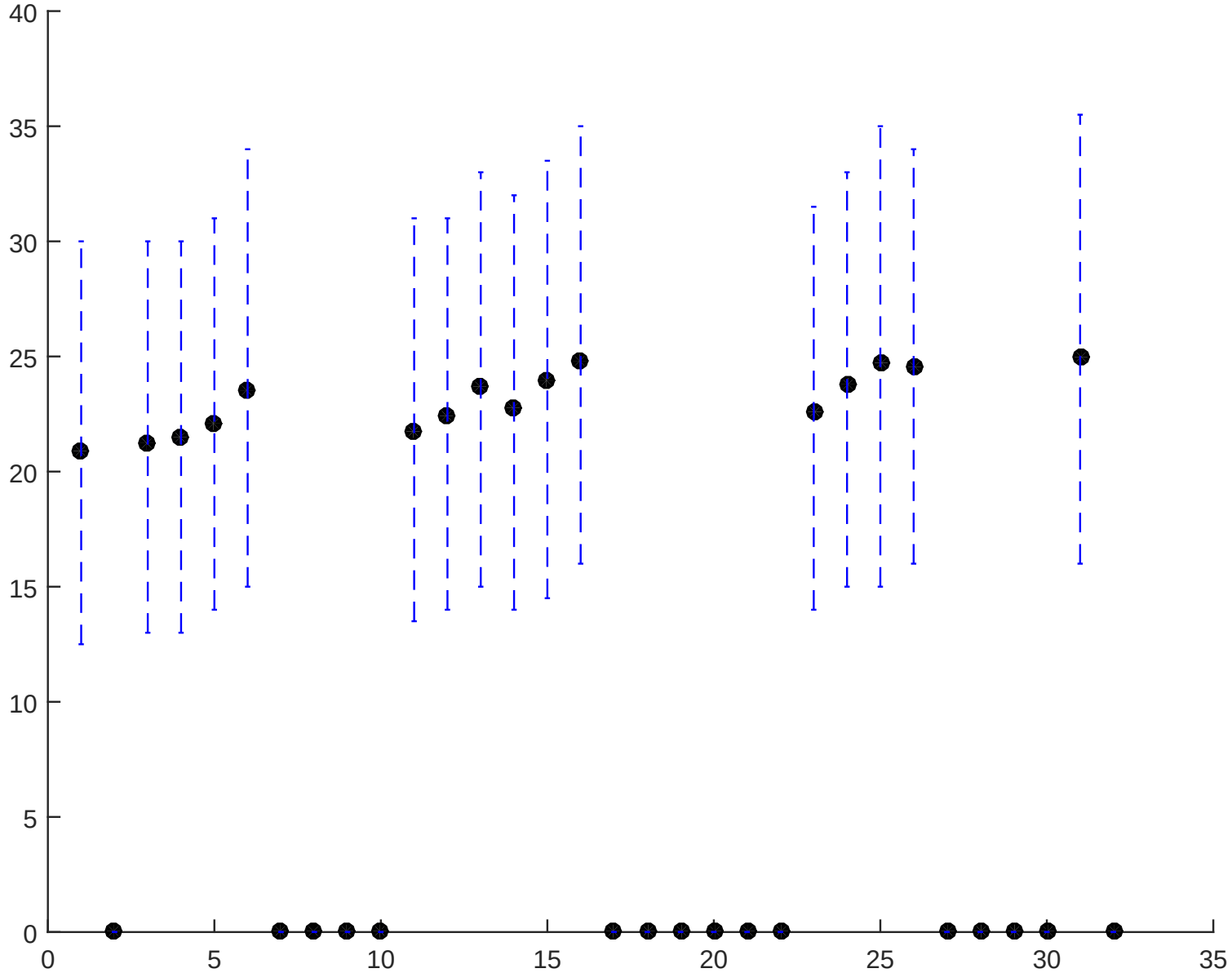
The performance of the interventions on the I_d outcome was very similar to that for the I_{xd} since the only transition to I_d is through I_{xd}, i.e. eliminating the I_{xd} would also eliminate the I_d population. As such, we see again that the SENS intervention singly is sufficient to control the I_d outcome (Supplementary Figure S22). The intervention comparisons were similar to those for the I_{xd} outcome.

Outcome	Ranking
AR	CP, COA, ENV, DECOL, SENS
	{COA, CP}, {ENV, CP}, {COA, ENV}, {CP, DECOL}, {CP, SENS}, {COA, DECOL}, {COA, SENS}, {ENV, DECOL}, {ENV, SENS}, {SENS, DECOL}
	{COA, ENV, CP}, {COA, CP, DECOL}, {COA, CP, SENS}, {ENV, CP, DECOL}, {ENV, CP, SENS}, {COA, ENV, DECOL}, {COA, ENV, SENS}, {CP, SENS, DECOL}, {ENV, SENS, DECOL}, {COA, SENS, DECOL}
	{COA, ENV, CP, DECOL}, {COA, ENV, CP, SENS}, {ENV, CP, SENS, DECOL}, {COA, CP, SENS, DECOL}, {COA, ENV, SENS, DECOL}
AC	COA, ENV, CP, SENS, DECOL
	{COA, ENV}, {COA, CP}, {COA, SENS}, {COA, DECOL}, {ENV, CP}, {ENV, SENS}, {CP, SENS}, {ENV, DECOL}, {CP, DECOL}, {SENS, DECOL}
	{COA, ENV, CP}, {COA, ENV, SENS}, {COA, ENV, DECOL}, {COA, CP, SENS}, {COA, CP, DECOL}, {COA, SENS, DECOL}, {ENV, CP, SENS}, {ENV, CP, DECOL}, {CP, SENS, DECOL}, {ENV, SENS, DECOL}
	{COA, ENV, CP, SENS}, {COA, ENV, CP, DECOL}, {COA, ENV, SENS, DECOL}, {COA, CP, SENS, DECOL}, {ENV, CP, SENS, DECOL}
C_{xd}	CP, ENV, COA, SENS, DECOL
	{COA, CP}, {ENV, CP}, {CP, SENS}, {COA, ENV}, {CP, DECOL}, {ENV, SENS}, {ENV, DECOL}, {COA, SENS}, {COA, DECOL}, {SENS, DECOL}
	{COA, ENV, CP}, {ENV, CP, SENS}, {ENV, CP, DECOL}, {COA, CP, DECOL}, {COA, CP, SENS}, {COA, ENV, SENS}, {COA, ENV, DECOL}, {CP, SENS, DECOL}, {ENV, SENS, DECOL}, {COA, SENS, DECOL}
	{COA, ENV, CP, DECOL}, {COA, ENV, CP, SENS}, {ENV, CP, SENS, DECOL}, {COA, CP, SENS, DECOL}, {COA, ENV, SENS, DECOL}
C_d	COA, CP, ENV, SENS, DECOL
	{COA, CP}, {COA, ENV}, {COA, DECOL}, {COA, SENS}, {ENV, CP}, {CP, SENS}, {CP, DECOL}, {ENV, SENS}, {ENV, DECOL}, {SENS, DECOL}
	{COA, ENV, CP}, {COA, CP, DECOL}, {COA, CP, SENS}, {COA, ENV, DECOL}, {COA, ENV, SENS}, {COA, SENS, DECOL}, {ENV, CP, SENS}, {ENV, CP, DECOL}, {CP, SENS, DECOL}, {ENV, SENS, DECOL}
	{COA, ENV, CP, DECOL}, {COA, ENV, CP, SENS}, {COA, CP, SENS, DECOL}, {COA, ENV, SENS, DECOL}, {ENV, CP, SENS, DECOL}
I_{xd}	SENS, COA, CP, ENV, DECOL
	{COA, SENS}, {ENV, SENS}, {CP, SENS}, {SENS, DECOL}, {COA, CP}, {COA, ENV}, {COA, DECOL}, {ENV, CP}, {ENV, DECOL}, {CP, DECOL}
	{COA, ENV, SENS}, {COA, CP, SENS}, {COA, SENS, DECOL}, {ENV, CP, SENS}, {ENV, SENS, DECOL}, {CP, SENS, DECOL}, {COA, ENV, CP}, {COA, CP, DECOL}, {COA, ENV, DECOL}, {ENV, CP, DECOL}
	{COA, ENV, CP, SENS}, {COA, ENV, SENS, DECOL}, {COA, CP, SENS, DECOL}, {ENV, CP, SENS, DECOL}, {COA, ENV, CP, DECOL}
I_d	SENS, COA, CP, ENV, DECOL
	{COA, SENS}, {ENV, SENS}, {CP, SENS}, {SENS, DECOL}, {COA, CP}, {COA, ENV}, {COA, DECOL}, {ENV, CP}, {ENV, DECOL}, {CP, DECOL}
	{COA, ENV, SENS}, {COA, CP, SENS}, {COA, SENS, DECOL}, {ENV, CP, SENS}, {ENV, SENS, DECOL}, {CP, SENS, DECOL}, {COA, ENV, CP}, {COA, CP, DECOL}, {COA, ENV, DECOL}, {ENV, CP, DECOL}
	{COA, ENV, CP, SENS}, {COA, ENV, SENS, DECOL}, {COA, CP, SENS, DECOL}, {ENV, CP, SENS, DECOL}, {COA, ENV, CP, DECOL}

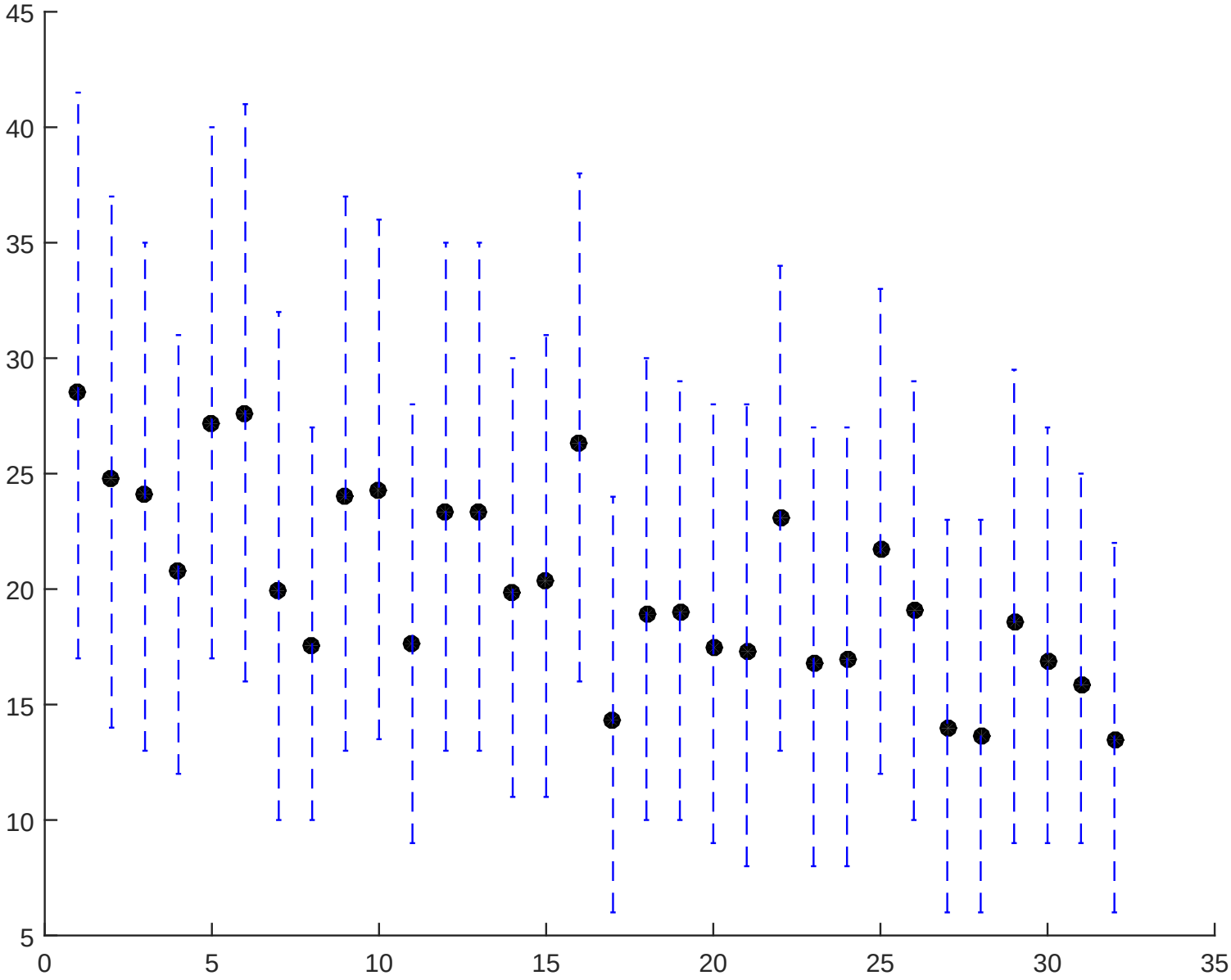
Supplementary Table S2: Ranking of the various intervention combinations by the output measure means and intervention sizes.



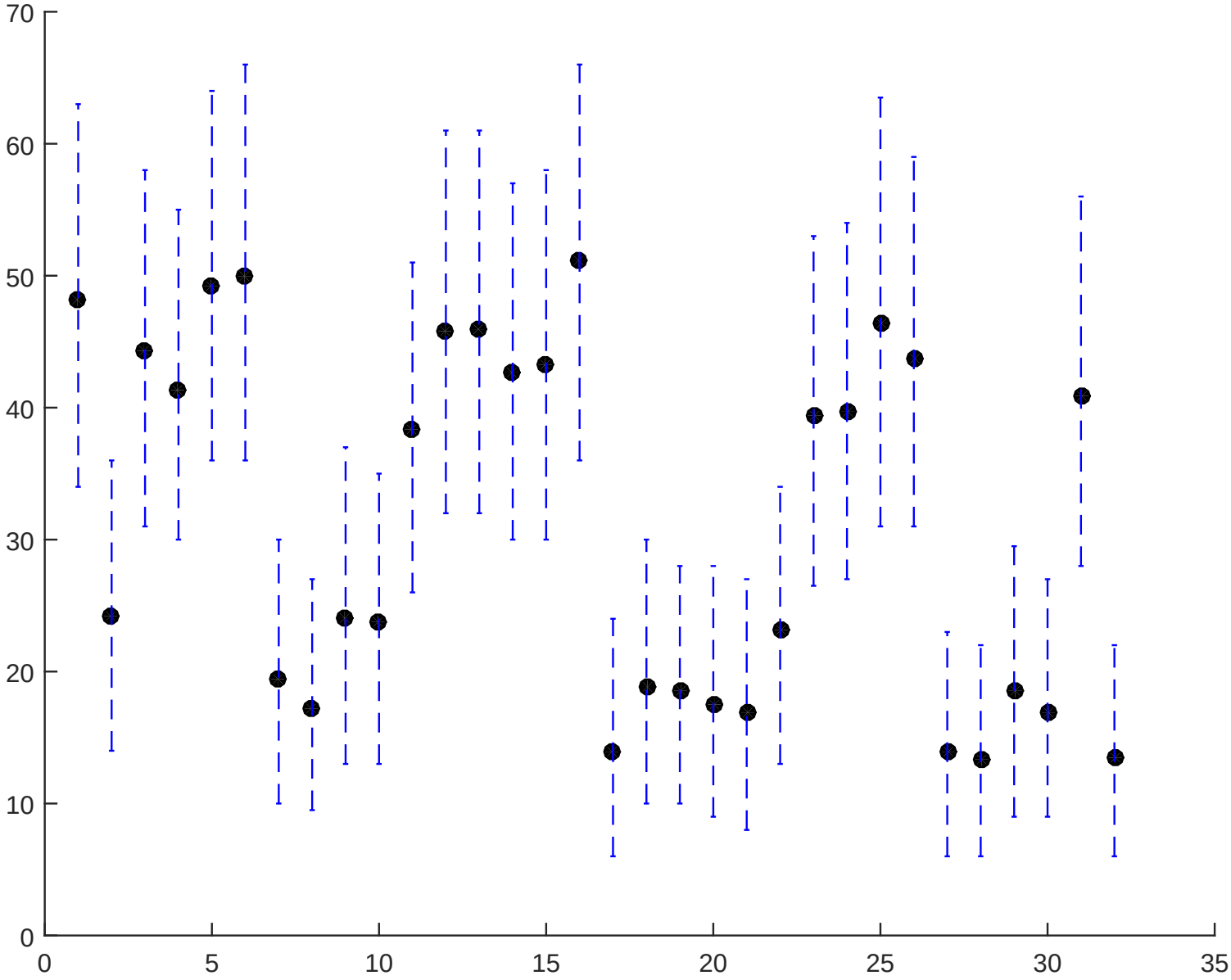
Supplementary Figure S17: Attack ratio average and 95% intervals in the simulated ward.



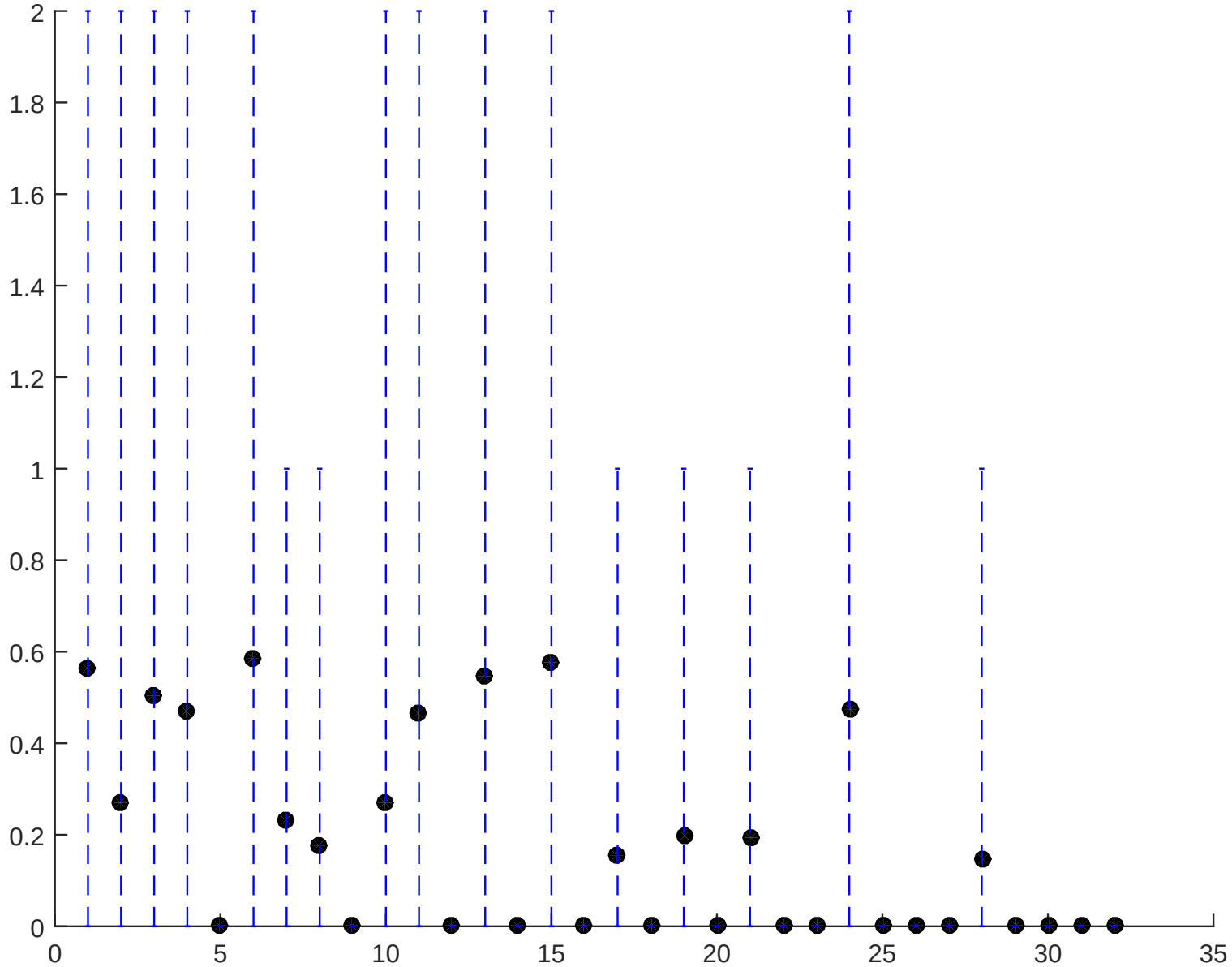
Supplementary Figure S18: AC average and 95% intervals in the simulated ward.



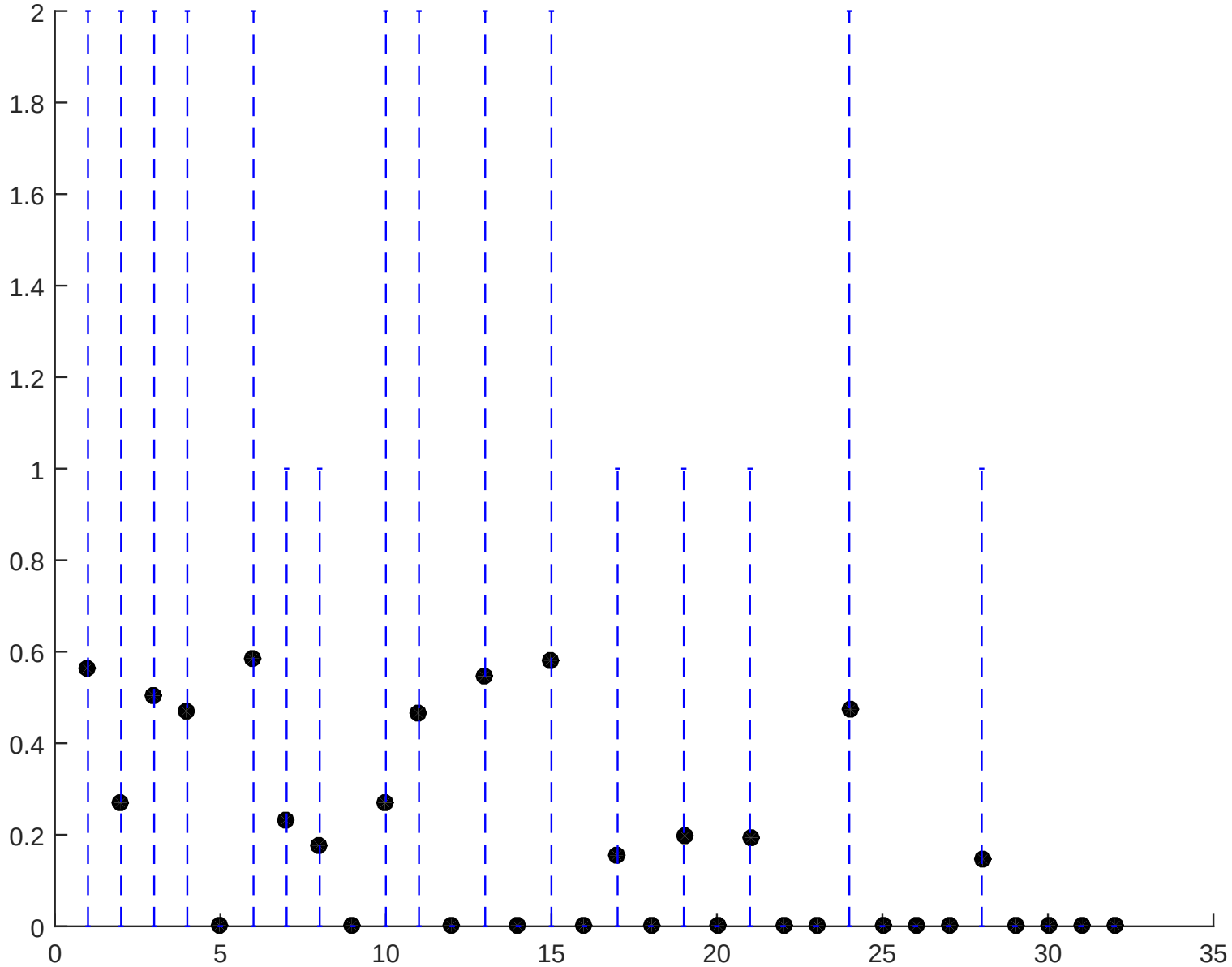
Supplementary Figure S19: C_{xd} average and 95% intervals in the simulated ward.



Supplementary Figure S20: C_d average and 95% intervals in the simulated ward.



Supplementary Figure S21: I_{xd} average and 95% intervals in the simulated ward.



Supplementary Figure S22: I_d average and 95% intervals in the simulated ward.

Comparison	AR $\hat{\theta}$ (95% CI)
COA v baseline	0.03 (0.02 , 0.03)
ENV v baseline	0.08 (0.07 , 0.09)
CP v baseline	0.00 (0.00 , 0.00)
SENS v baseline	0.25 (0.23 , 0.27)
DECOL v baseline	0.20 (0.18 , 0.22)
CP v COA	0.18 (0.16 , 0.20)
CP v ENV	0.08 (0.07 , 0.09)
CP v SENS	0.00 (0.00 , 0.01)
CP v DECOL	0.01 (0.01 , 0.02)
{COA, CP} v {ENV, CP}	0.25 (0.23 , 0.27)
{COA, CP} v {COA, ENV}	0.16 (0.14 , 0.17)
{COA, CP} v {CP, DECOL}	0.07 (0.06 , 0.08)
{COA, CP} v {CP, SENS}	0.04 (0.04 , 0.05)
{COA, ENV, CP} v {COA, CP, DECOL}	0.09 (0.07 , 0.10)
{COA, ENV, CP} v {COA, CP, SENS}	0.07 (0.06 , 0.08)
{COA, ENV, CP} v {ENV, CP, DECOL}	0.06 (0.05 , 0.07)
{COA, ENV, CP} v {ENV, CP, SENS}	0.04 (0.03 , 0.05)
{COA, ENV, CP, DECOL} v {COA, ENV, CP, SENS}	0.43 (0.41 , 0.46)
{COA, ENV, CP, DECOL} v {COA, ENV, SENS, DECOL}	0.01 (0.01 , 0.01)
{COA, ENV, CP, DECOL} v {COA, CP, SENS, DECOL}	0.04 (0.03 , 0.05)
{COA, ENV, CP, DECOL} v {ENV, CP, SENS, DECOL}	0.04 (0.04 , 0.06)
{COA, CP} v CP	0.02 (0.01 , 0.03)
{COA, ENV, CP} v {COA, CP}	0.04 (0.04 , 0.06)
{COA, ENV, CP, DECOL} v {COA, ENV, CP}	0.33 (0.30 , 0.35)
{COA, ENV, CP, SENS} v {COA, ENV, CP}	0.38 (0.35 , 0.40)
all v {COA, ENV, CP}	0.20 (0.18 , 0.22)
all v {COA, ENV, CP, DECOL}	0.35 (0.33 , 0.38)
all v {COA, ENV, CP, SENS}	0.28 (0.26 , 0.30)

Supplementary Table S3: θ estimates for AR comparisons of intervention combinations.

Comparison	AC $\hat{\theta}$ (95% CI)
COA v baseline	0.00 (0.00 , 0.00)
ENV v baseline	0.52 (0.50 , 0.55)
CP v baseline	0.54 (0.51 , 0.57)
SENS v baseline	0.57 (0.54 , 0.59)
DECOL v baseline	0.65 (0.63 , 0.68)
COA v ENV	0.00 (0.00 , 0.00)
COA v CP	0.00 (0.00 , 0.00)
COA v SENS	0.00 (0.00 , 0.00)
COA v DECOL	0.00 (0.00 , 0.00)
{COA, .} v {ENV, CP}	0.00 (0.00 , 0.00)
{COA, .} v {ENV, SENS}	0.00 (0.00 , 0.00)
{COA, .} v {CP, SENS}	0.00 (0.00 , 0.00)
{COA, .} v {ENV, DECOL}	0.00 (0.00 , 0.00)
{COA, .} v {CP, DECOL}	0.00 (0.00 , 0.00)
{COA, .} v {SENS, DECOL}	0.00 (0.00 , 0.00)
{COA, ., .} v {ENV, CP, SENS}	0.00 (0.00 , 0.00)
{COA, ., .} v {ENV, CP, DECOL}	0.00 (0.00 , 0.00)
{COA, ., .} v {CP, SENS, DECOL}	0.00 (0.00 , 0.00)
{COA, ., .} v {ENV, SENS, DECOL}	0.00 (0.00 , 0.00)
{COA, ., ., .} v {ENV, CP, SENS, DECOL}	0.00 (0.00 , 0.00)

Supplementary Table S4: θ estimates for AC comparisons of intervention combinations.

Comparison	C_{xd} $\hat{\theta}$ (95% CI)
COA v baseline	0.33 (0.31 , 0.35)
ENV v baseline	0.30 (0.28 , 0.32)
CP v baseline	0.17 (0.15 , 0.19)
SENS v baseline	0.43 (0.41 , 0.46)
DECOL v baseline	0.45 (0.43 , 0.48)
CP v COA	0.30 (0.28 , 0.32)
CP v ENV	0.33 (0.31 , 0.35)
CP v SENS	0.20 (0.19 , 0.23)
CP v DECOL	0.20 (0.18 , 0.22)
{COA, CP} v {ENV, CP}	0.50 (0.47 , 0.52)
{COA, CP} v {CP, SENS}	0.37 (0.35 , 0.39)
{COA, CP} v {COA, ENV}	0.37 (0.35 , 0.40)
{COA, CP} v {CP, DECOL}	0.35 (0.32 , 0.37)
{COA, CP} v {ENV, SENS}	0.21 (0.20 , 0.24)
{COA, CP} v {ENV, DECOL}	0.22 (0.20 , 0.24)
{COA, CP} v {COA, SENS}	0.20 (0.18 , 0.22)
{COA, CP} v {COA, DECOL}	0.19 (0.17 , 0.21)
{COA, CP} v {SENS, DECOL}	0.12 (0.10 , 0.13)
{COA, ENV, CP} v {ENV, CP, SENS}	0.35 (0.32 , 0.37)
{COA, ENV, CP} v {ENV, CP, DECOL}	0.34 (0.32 , 0.36)
{COA, ENV, CP} v {COA, CP, DECOL}	0.32 (0.30 , 0.35)
{COA, ENV, CP} v {COA, CP, SENS}	0.32 (0.29 , 0.34)
{COA, ENV, CP} v {COA, ENV, SENS}	0.25 (0.23 , 0.27)
{COA, ENV, CP} v {COA, ENV, DECOL}	0.24 (0.22 , 0.26)
{COA, ENV, CP} v {CP, SENS, DECOL}	0.23 (0.21 , 0.25)
{COA, ENV, CP} v {ENV, SENS, DECOL}	0.15 (0.13 , 0.17)
{COA, ENV, CP} v {COA, SENS, DECOL}	0.11 (0.09 , 0.12)
{COA, ENV, CP, DECOL} v {COA, ENV, CP, SENS}	0.48 (0.46 , 0.51)
{COA, ENV, CP, DECOL} v {ENV, CP, SENS, DECOL}	0.36 (0.34 , 0.38)
{COA, ENV, CP, DECOL} v {COA, CP, SENS, DECOL}	0.30 (0.28 , 0.33)
{COA, ENV, CP, DECOL} v {COA, ENV, SENS, DECOL}	0.23 (0.21 , 0.25)
{COA, ENV, CP, SENS} v {ENV, CP, SENS, DECOL}	0.38 (0.36 , 0.40)
{COA, ENV, CP, SENS} v {COA, CP, SENS, DECOL}	0.32 (0.30 , 0.35)
{COA, ENV, CP, SENS} v {COA, ENV, SENS, DECOL}	0.24 (0.22 , 0.26)
{COA, CP} v CP	0.32 (0.30 , 0.35)
{ENV, CP} v CP	0.33 (0.30 , 0.35)
{COA, ENV, CP} v {COA, CP}	0.30 (0.28 , 0.33)
{COA, ENV, CP} v {ENV, CP}	0.31 (0.29 , 0.33)
{COA, ENV, CP, DECOL} v {COA, ENV, CP}	0.46 (0.44 , 0.49)
{COA, ENV, CP, SENS} v {COA, ENV, CP}	0.48 (0.46 , 0.51)
all v {COA, ENV, CP}	0.45 (0.42 , 0.47)
all v {COA, ENV, CP, DECOL}	0.49 (0.46 , 0.51)
all v {COA, ENV, CP, SENS}	0.47 (0.44 , 0.49)

Supplementary Table S5: θ estimates for C_{xd} comparisons of intervention combinations.

Comparison	C_d $\hat{\theta}$ (95% CI)
COA v baseline	0.01 (0.00 , 0.01)
ENV v baseline	0.35 (0.32 , 0.37)
CP v baseline	0.24 (0.22 , 0.26)
SENS v baseline	0.53 (0.51 , 0.56)
DECOL v baseline	0.56 (0.53 , 0.58)
COA v CP	0.02 (0.02 , 0.03)
COA v ENV	0.01 (0.01 , 0.02)
COA v SENS	0.00 (0.00 , 0.01)
COA v DECOL	0.00 (0.00 , 0.01)
{COA, CP} v {COA, ENV}	0.38 (0.35 , 0.40)
{COA, CP} v {COA, DECOL}	0.19 (0.17 , 0.21)
{COA, CP} v {COA, SENS}	0.18 (0.16 , 0.20)
{COA, CP} v {ENV, CP}	0.00 (0.00 , 0.01)
{COA, ENV, CP} v {COA, CP, DECOL}	0.33 (0.30 , 0.35)
{COA, ENV, CP} v {COA, CP, SENS}	0.30 (0.28 , 0.32)
{COA, ENV, CP} v {COA, ENV, DECOL}	0.24 (0.22 , 0.26)
{COA, ENV, CP} v {COA, ENV, SENS}	0.24 (0.22 , 0.26)
{COA, ENV, CP} v {COA, SENS, DECOL}	0.10 (0.08 , 0.11)
{COA, ENV, CP, DECOL} v {COA, ENV, CP, SENS}	0.46 (0.43 , 0.48)
{COA, ENV, CP, DECOL} v {COA, CP, SENS, DECOL}	0.29 (0.26 , 0.31)
{COA, ENV, CP, DECOL} v {COA, ENV, SENS, DECOL}	0.21 (0.19 , 0.23)
{COA, ENV, CP, DECOL} v {ENV, CP, SENS, DECOL}	0.00 (0.00 , 0.00)
{COA, ENV, CP, SENS} v {COA, CP, SENS, DECOL}	0.32 (0.30 , 0.35)
{COA, ENV, CP, SENS} v {COA, ENV, SENS, DECOL}	0.24 (0.22 , 0.26)
{COA, ENV, CP, SENS} v {ENV, CP, SENS, DECOL}	0.00 (0.00 , 0.00)
{COA, CP} v COA	0.17 (0.15 , 0.19)
{COA, ENV, CP} v {COA, CP}	0.31 (0.28 , 0.33)
{COA, ENV, CP, DECOL} v {COA, ENV, CP}	0.46 (0.44 , 0.49)
{COA, ENV, CP, SENS} v {COA, ENV, CP}	0.50 (0.48 , 0.53)
all v {COA, ENV, CP}	0.47 (0.44 , 0.49)
all v {COA, ENV, CP, DECOL}	0.51 (0.48 , 0.53)
all v {COA, ENV, CP, SENS}	0.47 (0.44 , 0.49)

Supplementary Table S6: θ estimates for C_d comparisons of intervention combinations.

Comparison	I_{xd} $\hat{\theta}$ (95% CI)
COA v baseline	0.39 (0.37 , 0.42)
ENV v baseline	0.48 (0.45 , 0.50)
CP v baseline	0.47 (0.44 , 0.49)
SENS v baseline	0.28 (0.26 , 0.30)
DECOL v baseline	0.51 (0.48 , 0.53)
SENS v COA	0.38 (0.36 , 0.40)
SENS v CP	0.31 (0.29 , 0.33)
SENS v ENV	0.30 (0.28 , 0.33)
SENS v DECOL	0.28 (0.25 , 0.30)
COA v CP	0.42 (0.40 , 0.45)
COA v ENV	0.42 (0.39 , 0.44)
COA v DECOL	0.39 (0.36 , 0.41)
{SENS, .} v {COA, CP}	0.42 (0.40 , 0.45)
{SENS, .} v {COA, ENV}	0.40 (0.37 , 0.42)
{SENS, .} v {COA, DECOL}	0.39 (0.36 , 0.41)
{SENS, .} v {ENV, CP}	0.31 (0.29 , 0.33)
{SENS, .} v {ENV, DECOL}	0.28 (0.26 , 0.31)
{SENS, .} v {CP, DECOL}	0.28 (0.26 , 0.31)
{SENS, ., .} v {COA, ENV, CP}	0.43 (0.40 , 0.45)
{SENS, ., .} v {COA, CP, DECOL}	0.41 (0.39 , 0.44)
{SENS, ., .} v {COA, ENV, DECOL}	0.41 (0.39 , 0.44)
{SENS, ., .} v {ENV, CP, DECOL}	0.31 (0.29 , 0.33)
{SENS, ., ., .} v {COA, ENV, CP, DECOL}	0.43 (0.41 , 0.46)
{SENS, .} v SENS	0.50 (0.47 , 0.53)
{SENS, ., .} v SENS	0.50 (0.47 , 0.53)
{SENS, ., ., .} v SENS	0.50 (0.47 , 0.53)
all v SENS	0.50 (0.47 , 0.53)

Supplementary Table S7: θ estimates for I_{xd} comparisons of intervention combinations.

Comparison	I_d $\hat{\theta}$ (95% CI)
COA v baseline	0.40 (0.37 , 0.42)
ENV v baseline	0.48 (0.45 , 0.50)
CP v baseline	0.47 (0.44 , 0.49)
SENS v baseline	0.28 (0.26 , 0.30)
DECOL v baseline	0.51 (0.48 , 0.53)
SENS v COA	0.38 (0.36 , 0.40)
SENS v CP	0.31 (0.29 , 0.33)
SENS v ENV	0.30 (0.28 , 0.33)
SENS v DECOL	0.28 (0.26 , 0.30)
COA v CP	0.42 (0.40 , 0.45)
COA v ENV	0.42 (0.39 , 0.44)
COA v DECOL	0.39 (0.36 , 0.41)
{SENS, .} v {COA, CP}	0.42 (0.40 , 0.45)
{SENS, .} v {COA, ENV}	0.40 (0.37 , 0.42)
{SENS, .} v {COA, DECOL}	0.39 (0.36 , 0.41)
{SENS, .} v {ENV, CP}	0.31 (0.29 , 0.33)
{SENS, .} v {ENV, DECOL}	0.28 (0.26 , 0.31)
{SENS, .} v {CP, DECOL}	0.28 (0.26 , 0.31)
{SENS, ., .} v {COA, ENV, CP}	0.43 (0.40 , 0.45)
{SENS, ., .} v {COA, CP, DECOL}	0.41 (0.39 , 0.44)
{SENS, ., .} v {COA, ENV, DECOL}	0.41 (0.39 , 0.44)
{SENS, ., .} v {ENV, CP, DECOL}	0.31 (0.29 , 0.33)
{SENS, ., ., .} v {COA, ENV, CP, DECOL}	0.44 (0.41 , 0.46)
{SENS, .} v SENS	0.50 (0.47 , 0.53)
{SENS, ., .} v SENS	0.50 (0.47 , 0.53)
{SENS, ., ., .} v SENS	0.50 (0.47 , 0.53)
all v SENS	0.50 (0.47 , 0.53)

Supplementary Table S8: θ estimates for I_d comparisons of intervention combinations.

E Additional results for high burden setting

Supplementary Figures S23, S24, S25, S26, S27 and S28 have the same x-axis label ordering as the corresponding plots in the normal burden setting (see Section D).

E.1 AR outcome

For the AR outcome measure in the high burden setting, all single interventions produced a reduced AR distribution compared with the baseline. The CP intervention performed the best out of all five single interventions, followed by the SENS intervention. The COA and ENV interventions performed similarly and the DECOL intervention produced the smallest reduction in the AR outcome (with $\hat{\theta} = 0.33(0.30, 0.35)$ when compared with baseline). The best performing single intervention (CP) also substantially outperform the four other single interventions with $\hat{\theta}$ ranging from 0.01 (for DECOL) to 0.16 (for SENS).

The best performing intervention pair for the AR outcome was {CP, SENS} outperforming the second best intervention pair ({COA, CP}) with $\hat{\theta}$ of $0.29(0.27, 0.32)$ and greatly outperforming the other intervention pairs (with the θ estimates for the next five best pairs provided in Supplementary Table S10).

The {COA, CP, SENS} intervention triplet produced the smallest average AR mean (7.88×10^{-3}) out of all intervention triplets. However there is little evidence of a distributional difference in the AR outcome when compared with the second best performing intervention triplet ({ENV, CP, SENS}) an estimated θ of $0.45(0.43, 0.48)$. There is a slight improvement when comparing the {COA, CP, SENS} triplet with the triplets with the third and fourth smallest AR mean ({CP, SENS, DECOL} with $\hat{\theta} = 0.26(0.24, 0.28)$ and {COA, ENV, CP} with $\hat{\theta} = 0.35(0.33, 0.38)$. The wider 95% interval for the AR outcome associated with {COA, ENV, CP} produced a distribution that was more similar (i.e. larger $\hat{\theta}$) to the {COA, CP, SENS} triplet compared with the {CP, SENS, DECOL} triplet. The comparisons between the {ENV, CP, SENS} triplet with the other triplets with a larger AR mean was similar to those for {COA, CP, SENS} albeit with slightly larger θ estimates.

The best performing quartet for the AR outcome was {COA, ENV, CP, SENS} which produced a substantially smaller AR outcome distribution compared with the other four intervention quartets tested (with $\hat{\theta}$ values between 0.02 and 0.20).

There were substantial reductions in the AR outcome distribution when moving from the best performing single intervention to the best performing intervention pair ($\hat{\theta} = 0.01(0.01, 0.02)$), from the best pair to either of the best performing triplets ($\hat{\theta}$ of either $0.03(0.02, 0.04)$ or $0.04(0.04, 0.05)$), and from either of the best performing triplets to the best performing quartet ($\hat{\theta}$ of $0.03(0.02, 0.04)$ in both comparisons). The reduction in the AR distribution when moving from the best performing quartet to all intervention was also significant but not as drastic as the other increases in intervention sizes ($\hat{\theta} = 0.16(0.15, 0.18)$).

E.2 AC outcome

As with the normal setting, the COA intervention was the most important intervention for the AC outcome as it eliminates the possibility of colonised patients being admitted. Any

intervention combination which include the COA intervention achieved 0 AC, whereas intervention combinations without the COA intervention produced AC distributions with 95% quantiles that do not include 0 (Supplementary Figure S24). This was also reflected in the θ estimates for the comparison of interventions combinations with the COA intervention against those without (Supplementary Table S11).

E.3 C_{xd} outcome

Comparison	C_{xd} $\hat{\theta}$ (95% CI)
COA v baseline	0.45 (0.42 , 0.47)
ENV v baseline	0.32 (0.30 , 0.35)
CP v baseline	0.09 (0.08 , 0.10)
SENS v baseline	0.43 (0.40 , 0.45)
DECOL v baseline	0.58 (0.56 , 0.61)
CP v ENV	0.18 (0.17 , 0.20)
CP v SENS	0.12 (0.11 , 0.14)
CP v COA	0.12 (0.10 , 0.13)
CP v DECOL	0.07 (0.06 , 0.08)
{ENV, CP} v {CP, SENS}	0.44 (0.41 , 0.46)
{ENV, CP} v {COA, CP}	0.40 (0.38 , 0.43)
{ENV, CP} v {CP, DECOL}	0.30 (0.27 , 0.32)
{ENV, CP} v {ENV, SENS}	0.17 (0.15 , 0.19)
{ENV, CP} v {COA, ENV}	0.16 (0.14 , 0.17)
{ENV, CP} v {COA, SENS}	0.12 (0.10 , 0.13)
{ENV, CP} v {ENV, DECOL}	0.07 (0.06 , 0.08)
{ENV, CP} v {SENS, DECOL}	0.06 (0.05 , 0.07)
{ENV, CP} v {COA, DECOL}	0.05 (0.04 , 0.06)
{ENV, CP, SENS} v {COA, ENV, CP}	0.48 (0.45 , 0.50)
{ENV, CP, SENS} v {COA, CP, SENS}	0.40 (0.38 , 0.43)
{ENV, CP, SENS} v {ENV, CP, DECOL}	0.32 (0.30 , 0.35)
{ENV, CP, SENS} v {CP, SENS, DECOL}	0.32 (0.29 , 0.34)
{ENV, CP, SENS} v {COA, CP, DECOL}	0.27 (0.25 , 0.29)
{ENV, CP, SENS} v {COA, ENV, SENS}	0.22 (0.20 , 0.24)
{ENV, CP, SENS} v {ENV, SENS, DECOL}	0.13 (0.11 , 0.15)
{ENV, CP, SENS} v {COA, ENV, DECOL}	0.09 (0.08 , 0.10)
{ENV, CP, SENS} v {COA, SENS, DECOL}	0.09 (0.08 , 0.11)
{COA, ENV, CP, SENS} v {ENV, CP, SENS, DECOL}	0.39 (0.37 , 0.42)
{COA, ENV, CP, SENS} v {COA, ENV, CP, DECOL}	0.36 (0.34 , 0.39)
{COA, ENV, CP, SENS} v {COA, CP, SENS, DECOL}	0.31 (0.29 , 0.33)
{COA, ENV, CP, SENS} v {COA, ENV, SENS, DECOL}	0.18 (0.16 , 0.20)
{ENV, CP} v CP	0.33 (0.31 , 0.36)
{CP, SENS} v CP	0.39 (0.37 , 0.42)
{COA, CP} v CP	0.43 (0.40 , 0.45)
{ENV, CP, SENS} v CP	0.19 (0.18 , 0.21)
{COA, ENV, CP} v CP	0.22 (0.20 , 0.24)

Continued on next page

Supplementary Table S12 – *Continued from previous page*

Comparison	C_{xd} $\hat{\theta}$ (95% CI)
{COA, CP, SENS} v CP	0.27 (0.25 , 0.30)
{ENV, CP, SENS} v {ENV, CP}	0.33 (0.31 , 0.36)
{COA, ENV, CP} v {ENV, CP}	0.36 (0.34 , 0.38)
{COA, CP, SENS} v {ENV, CP}	0.43 (0.40 , 0.45)
{ENV, CP, SENS} v {CP, SENS}	0.27 (0.25 , 0.30)
{COA, ENV, CP} v {CP, SENS}	0.30 (0.28 , 0.33)
{COA, CP, SENS} v {CP, SENS}	0.37 (0.34 , 0.39)
{ENV, CP, SENS} v {COA, CP}	0.25 (0.23 , 0.27)
{COA, ENV, CP} v {COA, CP}	0.28 (0.26 , 0.30)
{COA, CP, SENS} v {COA, CP}	0.34 (0.32 , 0.36)
{COA, ENV, CP, SENS} v {ENV, CP}	0.19 (0.17 , 0.21)
{COA, ENV, CP, SENS} v {CP, SENS}	0.15 (0.13 , 0.17)
{COA, ENV, CP, SENS} v {COA, CP}	0.14 (0.12 , 0.16)
{COA, ENV, CP, SENS} v {ENV, CP, SENS}	0.33 (0.30 , 0.35)
{COA, ENV, CP, SENS} v {COA, ENV, CP}	0.32 (0.29 , 0.34)
{COA, ENV, CP, SENS} v {COA, CP, SENS}	0.25 (0.23 , 0.27)
all v {ENV, CP}	0.13 (0.12 , 0.15)
all v {CP, SENS}	0.10 (0.09 , 0.12)
all v {COA, CP}	0.10 (0.08 , 0.11)
all v {ENV, CP, SENS}	0.25 (0.23 , 0.27)
all v {COA, ENV, CP}	0.24 (0.22 , 0.26)
all v {COA, CP, SENS}	0.18 (0.16 , 0.20)
all v {COA, ENV, CP, SENS}	0.42 (0.39 , 0.44)

Supplementary Table S12: θ estimates for C_{xd} comparisons of intervention combinations for high burden setting .

In the high burden setting, only the CP and ENV interventions singly produced C_{xd} outcome distributions which were smaller than the baseline scenario ($\hat{\theta}$ of $0.09(0.08, 0.10)$ for CP and $0.32(0.30, 0.35)$ for ENV). The other three interventions produced distributions which were similar to the baseline. The CP intervention also notably outperformed all other single interventions ($\hat{\theta}$ between 0.07 to 0.18).

The best performing intervention pair for this outcome is the {ENV, CP} pair. However, the {CP, SENS} and {COA, CP} intervention pairs have similar C_{xd} distributions as the {ENV, CP} pair (with $\hat{\theta}$ of $0.44(0.41, 0.46)$ and $0.40(0.38, 0.43)$ respectively). In short, the best preforming duos comprise of the CP intervention with either the ENV, SENS or COA intervention.

Following the similarity of the top three intervention duos, the best performing triplet was found to be {ENV, CP, SENS} followed by the triplets {COA, ENV, CP} and {COA, CP, SENS}. All three interventions had similar distributions. Again, we note that these triplet combinations are of CP with two of the three interventions which formed the top three best performing pairs (ENV, SENS or COA).

The intervention quartet which produced the smallest C_{xd} outcome distribution was the combination of the four interventions previously identified, namely {COA, ENV, CP, SENS}. There was only slight evidence that this intervention quartet performed better than the next three best performing quartets ({ENV, CP, SENS, DECOL} , {COA, ENV, CP, DECOL} and {COA, CP, SENS, DECOL} with $\hat{\theta}$ ranging between 0.31 to 0.39. However, the {COA, ENV, CP, SENS} quartet performed noticeably better when compared with the remaining quartet under consideration ({COA, ENV, SENS, DECOL} with $\hat{\theta} = 0.18(0.16, 0.20)$).

Comparing the top three intervention pairs with the best performing single intervention, there are slight gains, in terms of C_{xd} distribution reduction, in considering the {ENV, CP} or {CP, SENS} pairs rather than just CP singly ($\hat{\theta}$ of $0.33(0.30, 0.35)$ and $0.39(0.36, 0.41)$ respectively). The improvement in moving from CP to {COA, CP} was less noticeable ($\hat{\theta} = 0.43(0.41, 0.46)$).

Notable improvements were observed when moving from the CP intervention singly to the top three performing triplets ({ENV, CP, SENS}, {COA, CP, SENS},{COA, CP, SENS}) with θ estimates of between 0.19 to 0.27. However, the benefits from moving from one of the three intervention pairs identified to one of the three intervention triplets were less evident. There appears to be little gained in moving from the best performing pair ({ENV, CP}) to any of the triplets, particularly for {COA, CP, SENS} with $\hat{\theta} = 0.43(0.40, 0.45)$ (the other two triplets have $\hat{\theta}$ of $0.33(0.31, 0.36)$ and $0.36(0.34, 0.38)$). Improved performance was noted when moving from either of the other two pairs ({CP, SENS} or {COA, CP}) to either {ENV, CP, SENS} or {COA, ENV, CP} ($\hat{\theta}$ ranging from 0.25 to 0.30) but less so for a move to the {COA, CP, SENS} triplet (with $\hat{\theta}$ of $0.37(0.34, 0.39)$ and $0.34(0.32, 0.36)$ respectively).

The best performing quartet outperforms the top three intervention pairs with $\hat{\theta}$ ranging from 0.14 to 0.19. Gains from moving from one of the three triplets identified to the best performing quartet were marginal with the best improvement obtained when moving from {COA, CP, SENS} ($\hat{\theta} = 0.25(0.23, 0.27)$) and the least from {ENV, CP, SENS} with $\hat{\theta} = 0.33(0.30, 0.35)$.

The combination of all interventions performed better than all three interventions pairs ($\hat{\theta}$ ranging from 0.10 to 0.13) and the {COA, CP, SENS} triplet ($\hat{\theta} = 0.18(0.16, 0.20)$). It also outperformed the other two triplets ($\hat{\theta}$ of $0.2(0.23, 0.27)$ for {ENV, CP, SENS} and $0.24(0.22, 0.26)$ for {COA, ENV, CP}) but not the best performing quartet (with $\hat{\theta} = 0.42(0.39, 0.44)$).

E.4 C_d outcome

Of the five single interventions, only the COA and CP interventions produced C_d distributions smaller than the baseline. In fact, both these single interventions performed similarly to one another (with $\hat{\theta} = 0.45(0.42, 0.47)$), and outperforms the other three single interventions.

The best performing intervention pair was {COA, CP}, outperforming the other nine intervention pairs with the closest competitor being {COA, ENV} with $\hat{\theta} = 0.23(0.21, 0.25)$. The other pair comparisons with {COA, CP} resulted in θ estimates of between 0.00 to 0.13.

The {COA, ENV, CP} triplet produced the smallest C_d distribution of the intervention triplets, and was marginally better than the next two best performing triplets ({COA, CP, SENS} with $\hat{\theta}$ of $0.30(0.28, 0.33)$ and {COA, CP, DECOL} with $\hat{\theta}$ of 0.30 (0.27 , 0.32)). The {COA, ENV, CP} triplet performed more favourably when compared with the remaining

triplets, yielding θ estimates between 0.00 and 0.16.

The two best performing quartets for the C_d outcome measure were {COA, ENV, CP, SENS} and {COA, ENV, CP, DECOL} ($\hat{\theta} = 0.47(0.45, 0.50)$), followed closely by {COA, CP, SENS, DECOL} ($\hat{\theta}$ of $0.31(0.29, 0.33)$ for comparison with {COA, ENV, CP, SENS} and $0.33(0.31, 0.36)$ for comparison with {COA, ENV, CP, DECOL}). The other two quartets were less effective than {COA, ENV, CP, SENS} and {COA, ENV, CP, DECOL} in reducing the C_d outcome ($\hat{\theta}$ ranging from 0.02 to 0.21).

Comparing across intervention sizes, the {COA, CP} intervention pair was a drastic improvement from the COA intervention singly in terms of reduction in C_d distribution (with $\hat{\theta}$ of $0.08(0.07, 0.10)$). The best performing triplet provided a slight improvement compared with the {COA, CP} pair ($\hat{\theta} = 0.28(0.26, 0.30)$). The two best performing intervention quartets identified did not yield C_d distributions substantially different from that of the {COA, ENV, CP} triplets ($\hat{\theta}$ values of $0.41(0.39, 0.44)$ and $0.49(0.46, 0.51)$). These two quartets were still improvements over the best performing pair, but their comparative performance (with the pair) was similar to that of the best performing triplet (θ estimates of 0.21 and 0.27). While the combination of all five interventions provided a notable reduction in the C_d distribution from the best performing pair ($\hat{\theta} = 0.16(0.15, 0.18)$), it only performed marginally better than the {COA, ENV, CP} triplet and the {COA, ENV, CP, DECOL} quartet ($\hat{\theta}$ of $0.36(0.33, 0.38)$ and $0.37(0.35, 0.40)$ respectively) and offered a similar reduction in the C_d distribution as the {COA, ENV, CP, SENS} quartet $\hat{\theta} = 0.44(0.42, 0.47)$).

E.5 I_{xd} outcome

As with the normal burden setting, the SENS intervention was the most important intervention for the I_{xd} (and I_d) outcome(s) as having perfect sensitivity would allow detection of all colonised patients prior to infection developing. As such, the best performing intervention of any size will include the SENS intervention and are denoted by {SENS, .}, {SENS, ., .} and {SENS, ., ., .} to denote intervention pairs, triplets and quartets.

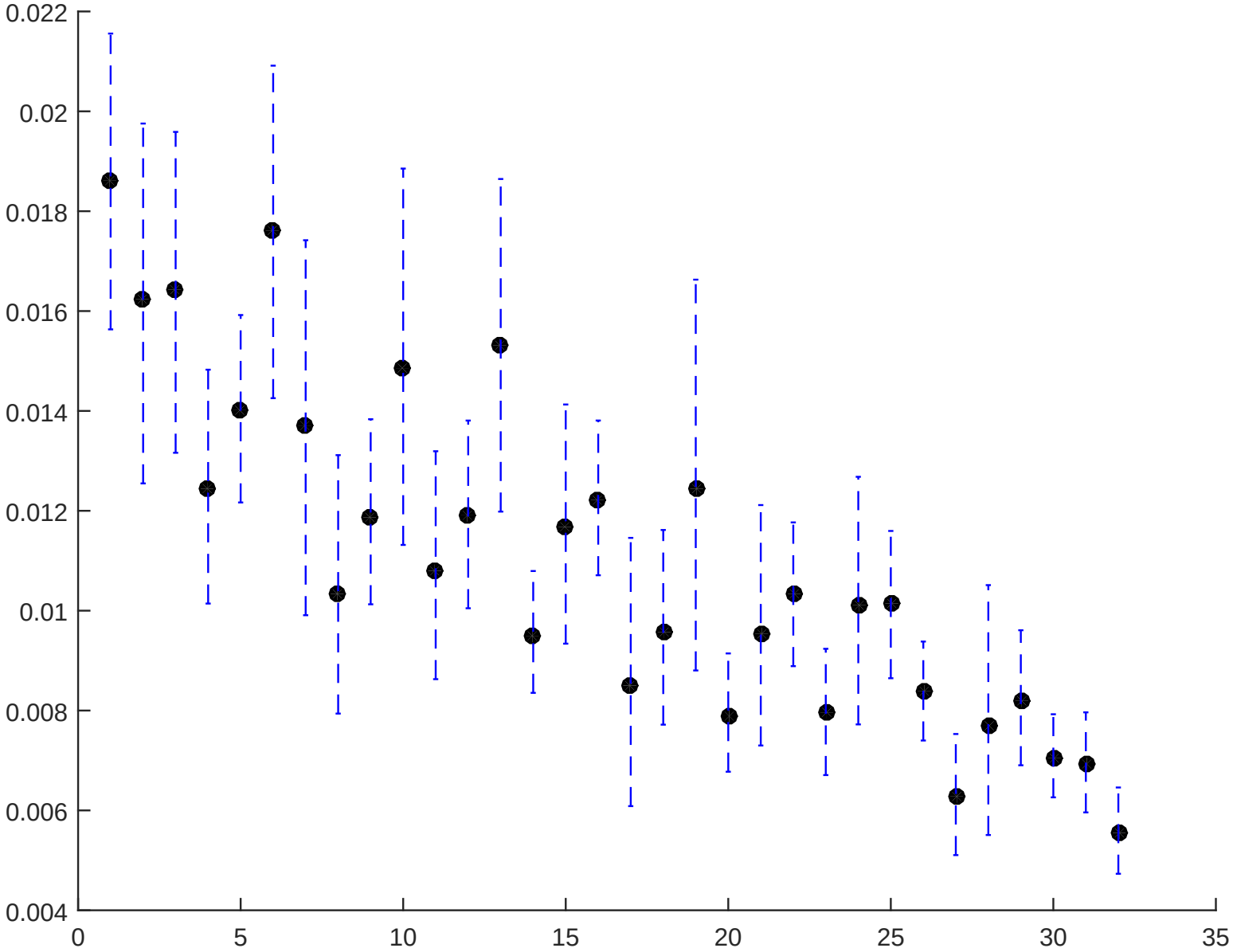
In contrast with the normal burden setting where the SENS intervention (of any size) only performed marginally better than the other intervention combinations despite completely removing any occurrence of I_{xd} patients as a result of the low baseline I_{xd} population, the SENS intervention (or any combination which includes the SENS intervention) was substantially more favourable in the high burden setting (Supplementary Figure S27). The SENS intervention substantially outperformed all intervention combinations which excluded the SENS intervention here (Supplementary Table S14).

E.6 I_d outcome

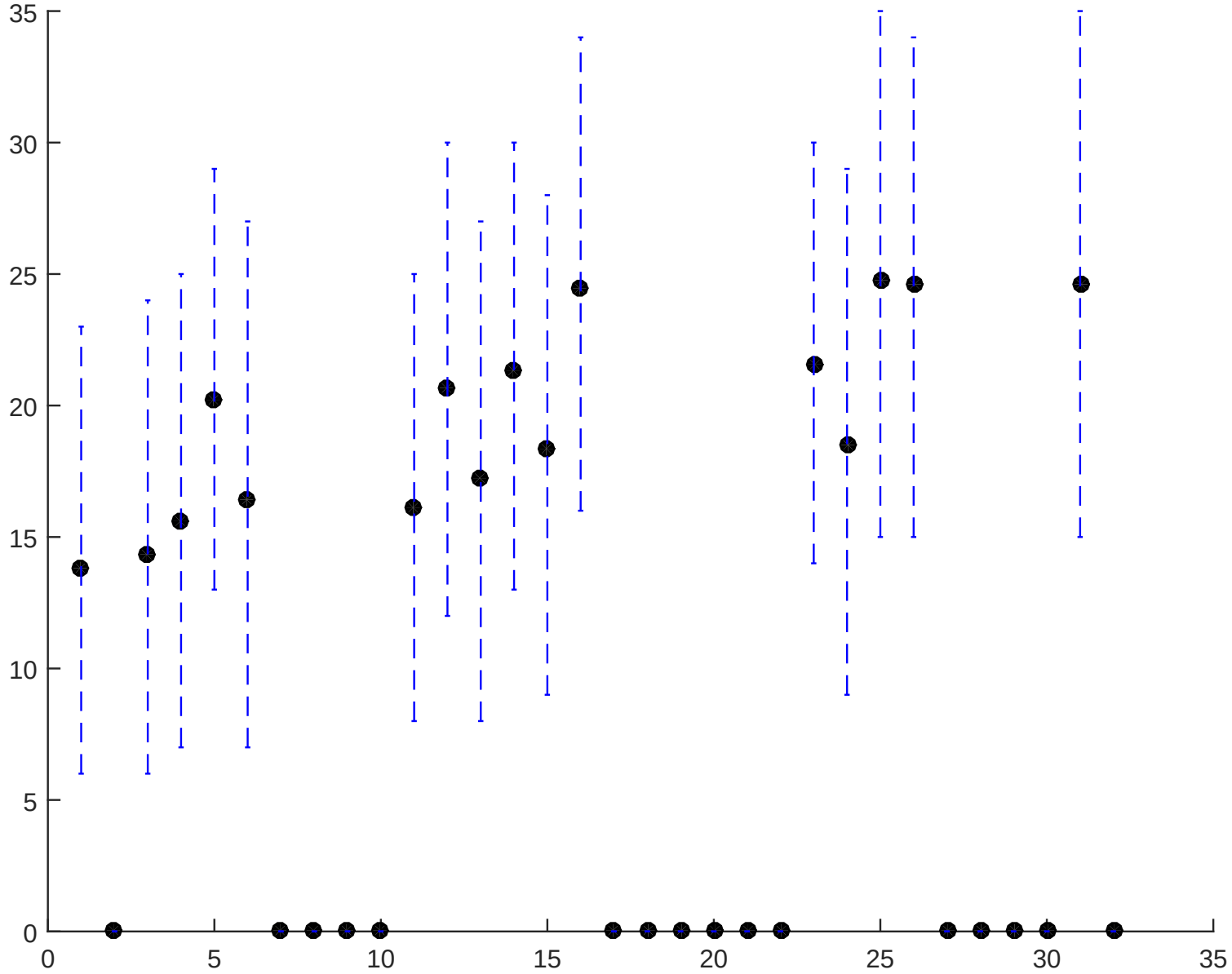
As with the I_{xd} outcome, the SENS intervention (or any intervention combination which included SENS) eradicated the I_d population and provided a drastic improvement from any intervention combinations which excluded the SENS intervention in the high burden setting (see Supplementary Figure S28 and Supplementary Table S15).

Outcome	Ranking
AR	CP, SENS, COA, ENV, DECOL
	{CP, SENS}, {COA, CP}, {ENV, CP}, {CP, DECOL}, {COA, SENS}, {ENV, SENS}, {SENS, DECOL}, {COA, ENV}, {COA, DECOL}, {ENV, DECOL}
	{COA, CP, SENS}, {ENV, CP, SENS}, {CP, SENS, DECOL}, {COA, ENV, CP}, {COA, CP, DECOL}, {COA, ENV, SENS}, {ENV, CP, DECOL}, {ENV, SENS, DECOL}, {COA, SENS, DECOL}, {COA, ENV, DECOL}
	{COA, ENV, CP, SENS}, {ENV, CP, SENS, DECOL}, {COA, CP, SENS, DECOL}, {COA, ENV, CP, DECOL}, {COA, ENV, SENS, DECOL}
AC	COA, ENV, CP, DECOL, SENS
	{COA, ENV}, {COA, CP}, {COA, SENS}, {COA, DECOL}, {ENV, CP}, {ENV, DECOL}, {CP, DECOL}, {ENV, SENS}, {CP, SENS}, {SENS, DECOL}
	{COA, ENV, CP}, {COA, ENV, SENS}, {COA, ENV, DECOL}, {COA, CP, SENS}, {COA, CP, DECOL}, {COA, SENS, DECOL}, {ENV, CP, DECOL}, {ENV, CP, SENS}, {CP, SENS, DECOL}, {ENV, SENS, DECOL}
	{COA, ENV, CP, SENS}, {COA, ENV, CP, DECOL}, {COA, ENV, SENS, DECOL}, {COA, CP, SENS, DECOL}, {ENV, CP, SENS, DECOL}
C_{xd}	CP, ENV, SENS, COA, DECOL
	{ENV, CP}, {CP, SENS}, {COA, CP}, {CP, DECOL}, {ENV, SENS}, {COA, ENV}, {COA, SENS}, {ENV, DECOL}, {SENS, DECOL}, {COA, DECOL}
	{ENV, CP, SENS}, {COA, ENV, CP}, {COA, CP, SENS}, {ENV, CP, DECOL}, {CP, SENS, DECOL}, {COA, CP, DECOL}, {COA, ENV, SENS}, {ENV, SENS, DECOL}, {COA, ENV, DECOL}, {COA, SENS, DECOL}
	{COA, ENV, CP, SENS}, {ENV, CP, SENS, DECOL}, {COA, ENV, CP, DECOL}, {COA, CP, SENS, DECOL}, {COA, ENV, SENS, DECOL}
C_d	COA, CP, ENV, DECOL, SENS
	{COA, CP}, {COA, ENV}, {ENV, CP}, {COA, SENS}, {COA, DECOL}, {CP, DECOL}, {CP, SENS}, {ENV, DECOL}, {ENV, SENS}, {SENS, DECOL}
	{COA, ENV, CP}, {COA, CP, SENS}, {COA, CP, DECOL}, {COA, ENV, SENS}, {COA, ENV, DECOL}, {COA, SENS, DECOL}, {ENV, CP, DECOL}, {ENV, CP, SENS}, {CP, SENS, DECOL}, {ENV, SENS, DECOL}
	{COA, ENV, CP, SENS}, {COA, ENV, CP, DECOL}, {COA, CP, SENS, DECOL}, {COA, ENV, SENS, DECOL}, {ENV, CP, SENS, DECOL}
I_{xd}	SENS, COA, CP, ENV, DECOL
	{COA, SENS}, {ENV, SENS}, {CP, SENS}, {SENS, DECOL}, {COA, CP}, {COA, ENV}, {ENV, CP}, {COA, DECOL}, {CP, DECOL}, {ENV, DECOL}
	{COA, ENV, SENS}, {COA, CP, SENS}, {COA, SENS, DECOL}, {ENV, CP, SENS}, {ENV, SENS, DECOL}, {CP, SENS, DECOL}, {COA, ENV, CP}, {COA, CP, DECOL}, {COA, ENV, DECOL}, {ENV, CP, DECOL}
	{COA, ENV, CP, SENS}, {COA, ENV, SENS, DECOL}, {COA, CP, SENS, DECOL}, {ENV, CP, SENS, DECOL}, {COA, ENV, CP, DECOL}
I_d	SENS, COA, CP, ENV, DECOL
	{COA, SENS}, {ENV, SENS}, {CP, SENS}, {SENS, DECOL}, {COA, CP}, {COA, ENV}, {ENV, CP}, {COA, DECOL}, {CP, DECOL}, {ENV, DECOL}
	{COA, ENV, SENS}, {COA, CP, SENS}, {COA, SENS, DECOL}, {ENV, CP, SENS}, {ENV, SENS, DECOL}, {CP, SENS, DECOL}, {COA, ENV, CP}, {COA, CP, DECOL}, {COA, ENV, DECOL}, {ENV, CP, DECOL}
	{COA, ENV, CP, SENS}, {COA, ENV, SENS, DECOL}, {COA, CP, SENS, DECOL}, {ENV, CP, SENS, DECOL}, {COA, ENV, CP, DECOL}

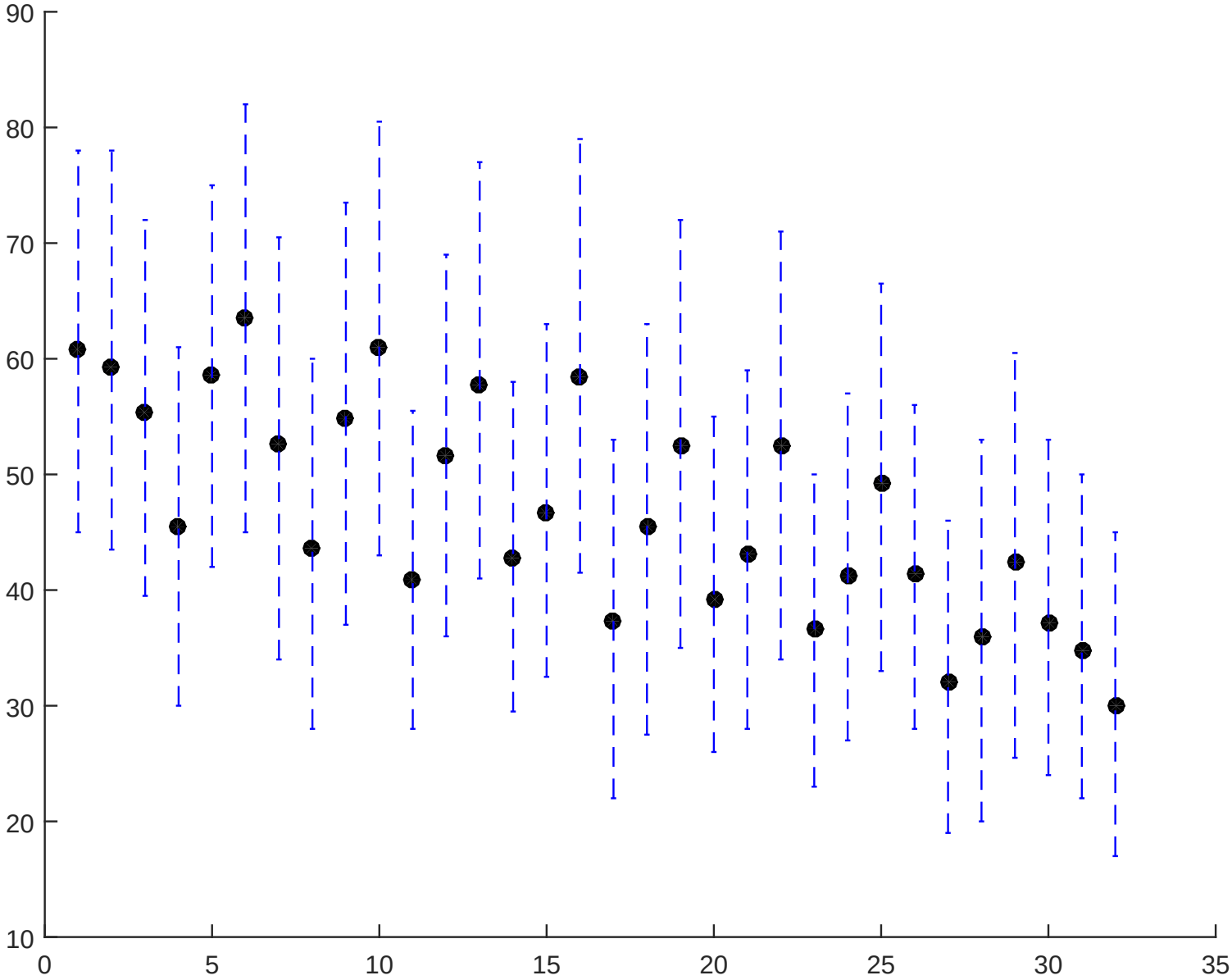
Supplementary Table S9: Ranking of the various intervention combinations by the output measure means and intervention sizes for the high burden setting.



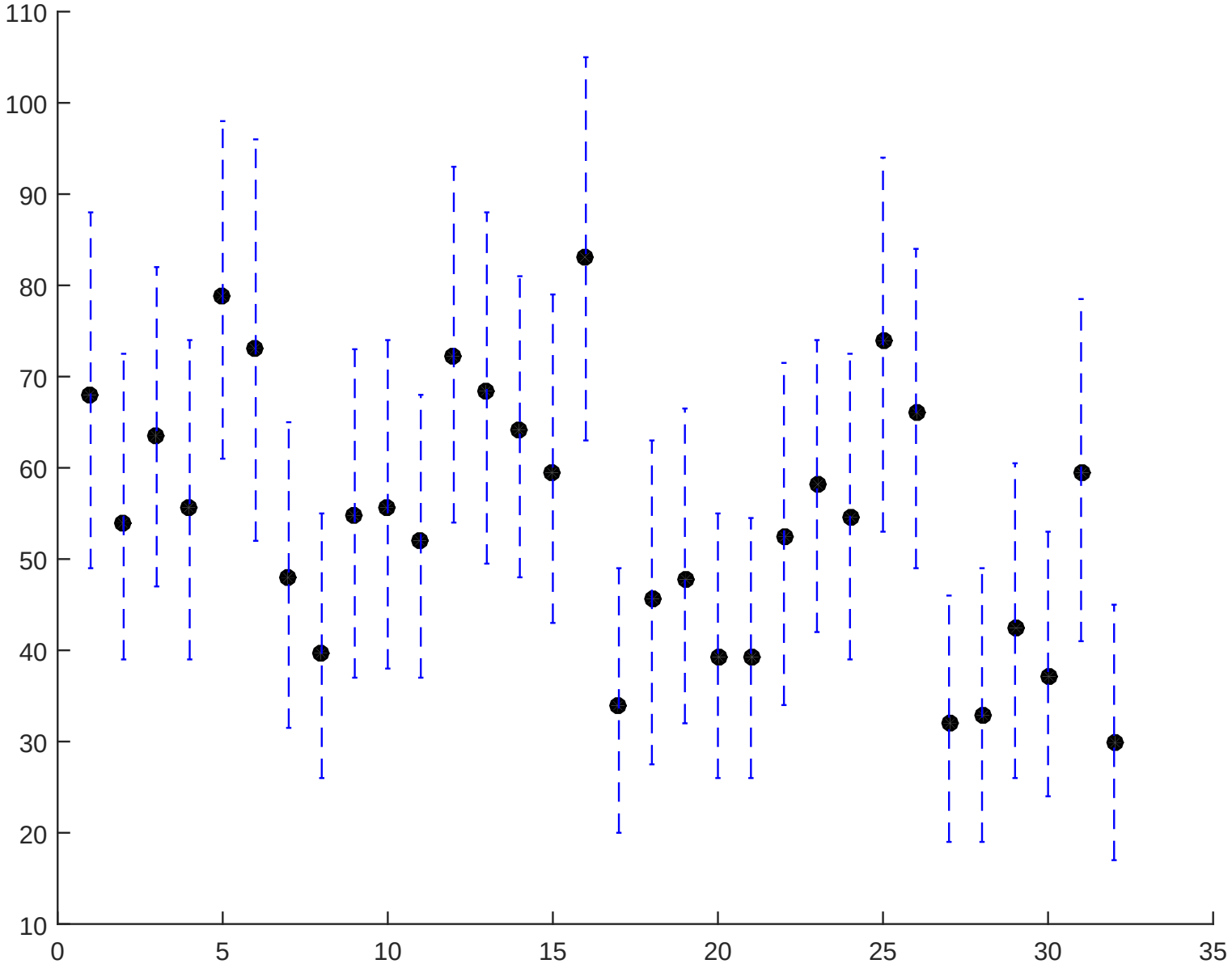
Supplementary Figure S23: Attack ratio average and 95% intervals in the simulated ward for the high burden setting.



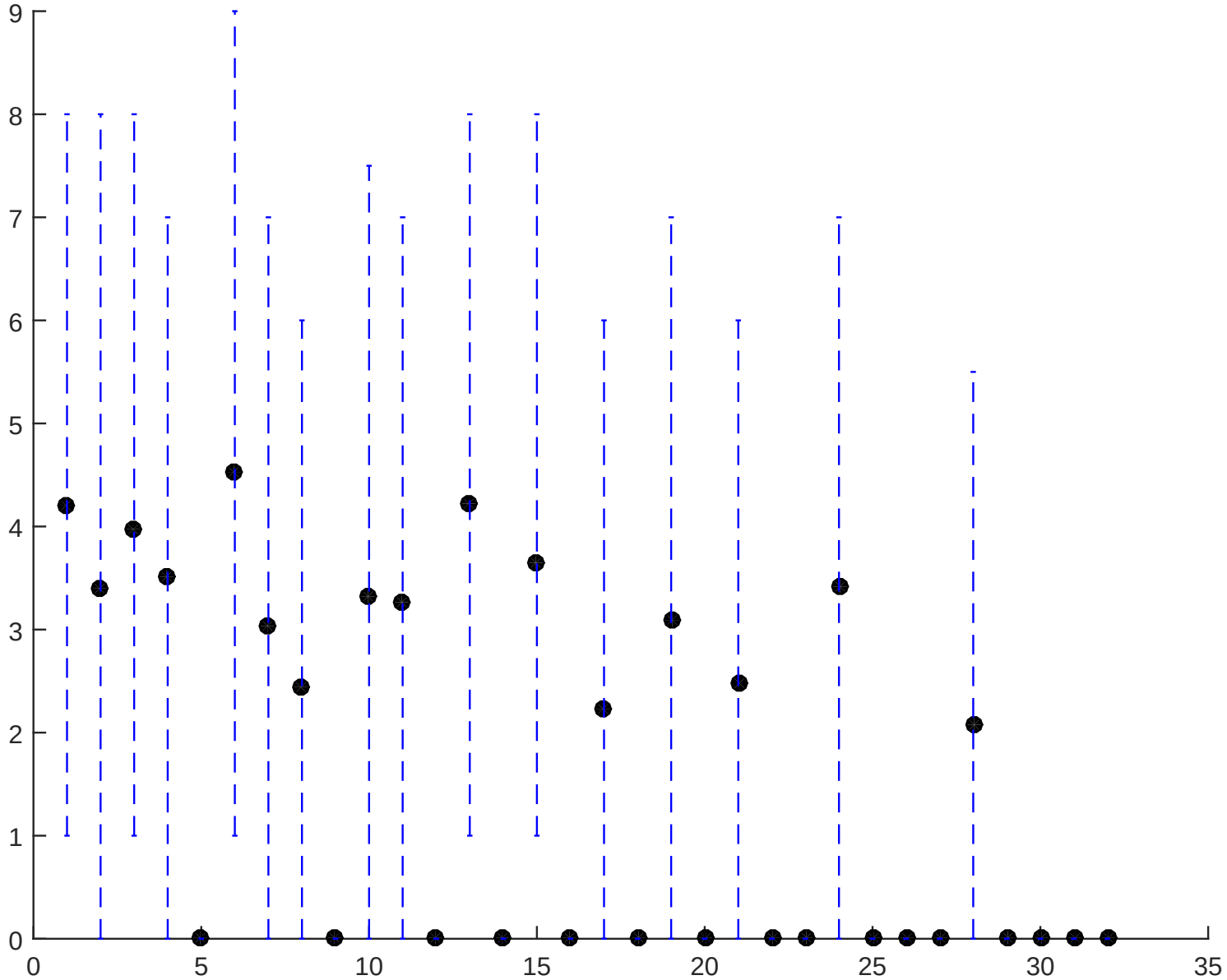
Supplementary Figure S24: AC average and 95% intervals in the simulated ward for the high burden setting.



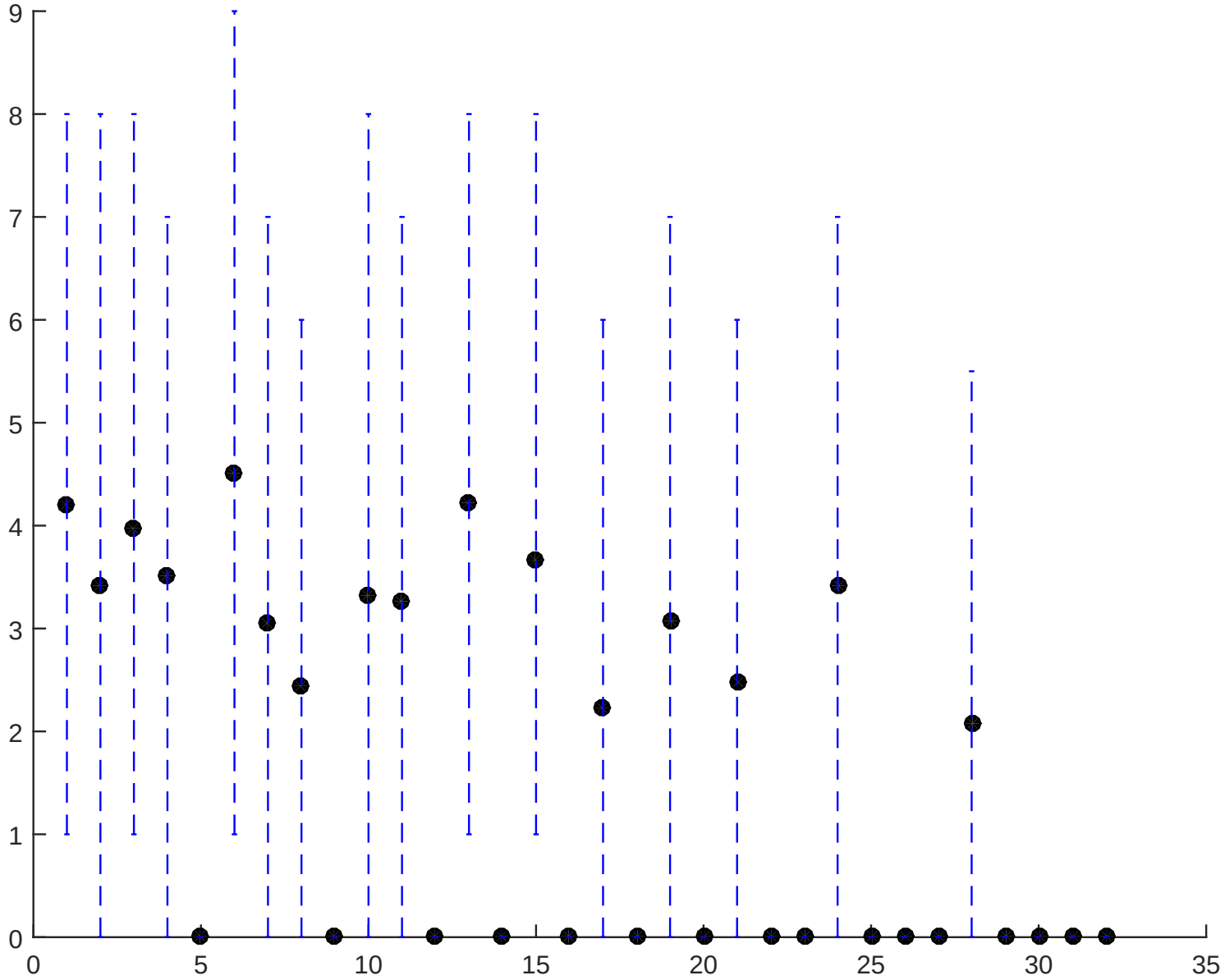
Supplementary Figure S25: C_{xd} average and 95% intervals in the simulated ward for the high burden setting.



Supplementary Figure S26: C_d average and 95% intervals in the simulated ward for the high burden setting.



Supplementary Figure S27: I_{xd} average and 95% intervals in the simulated ward for the high burden setting.



Supplementary Figure S28: I_d average and 95% intervals in the simulated ward for the high burden setting.

Comparison	AR $\hat{\theta}$ (95% CI)
COA v baseline	0.16 (0.15 , 0.18)
ENV v baseline	0.16 (0.15 , 0.18)
CP v baseline	0.00 (0.00 , 0.00)
SENS v baseline	0.00 (0.00 , 0.01)
DECOL v baseline	0.33 (0.30 , 0.35)
CP v SENS	0.16 (0.14 , 0.18)
CP v COA	0.05 (0.04 , 0.06)
CP v ENV	0.03 (0.02 , 0.04)
CP v DECOL	0.01 (0.00 , 0.01)
{CP, SENS} v {COA, CP}	0.29 (0.27 , 0.32)
{CP, SENS} v {ENV, CP}	0.17 (0.15 , 0.18)
{CP, SENS} v {CP, DECOL}	0.06 (0.05 , 0.07)
{CP, SENS} v {COA, SENS}	0.02 (0.01 , 0.02)
{CP, SENS} v {ENV, SENS}	0.02 (0.01 , 0.02)
{CP, SENS} v {SENS, DECOL}	0.00 (0.00 , 0.01)
{COA, CP, SENS} v {ENV, CP, SENS}	0.45 (0.43 , 0.48)
{COA, CP, SENS} v {CP, SENS, DECOL}	0.26 (0.24 , 0.28)
{COA, CP, SENS} v {COA, ENV, CP}	0.35 (0.33 , 0.38)
{COA, CP, SENS} v {COA, CP, DECOL}	0.12 (0.10 , 0.13)
{COA, CP, SENS} v {COA, ENV, SENS}	0.07 (0.06 , 0.08)
{COA, CP, SENS} v {ENV, CP, DECOL}	0.05 (0.04 , 0.06)
{COA, CP, SENS} v {ENV, SENS, DECOL}	0.01 (0.01 , 0.01)
{COA, CP, SENS} v {COA, SENS, DECOL}	0.01 (0.00 , 0.01)
{COA, CP, SENS} v {COA, ENV, DECOL}	0.01 (0.00 , 0.01)
{ENV, CP, SENS} v {CP, SENS, DECOL}	0.31 (0.29 , 0.34)
{ENV, CP, SENS} v {COA, ENV, CP}	0.38 (0.35 , 0.40)
{ENV, CP, SENS} v {COA, CP, DECOL}	0.14 (0.12 , 0.15)
{ENV, CP, SENS} v {COA, ENV, SENS}	0.09 (0.07 , 0.10)
{ENV, CP, SENS} v {ENV, CP, DECOL}	0.06 (0.05 , 0.07)
{ENV, CP, SENS} v {ENV, SENS, DECOL}	0.01 (0.01 , 0.02)
{ENV, CP, SENS} v {COA, SENS, DECOL}	0.01 (0.01 , 0.01)
{ENV, CP, SENS} v {COA, ENV, DECOL}	0.01 (0.01 , 0.01)
{COA, ENV, CP, SENS} v {ENV, CP, SENS, DECOL}	0.20 (0.18 , 0.22)
{COA, ENV, CP, SENS} v {COA, CP, SENS, DECOL}	0.15 (0.13 , 0.17)
{COA, ENV, CP, SENS} v {COA, ENV, CP, DECOL}	0.15 (0.13 , 0.17)
{COA, ENV, CP, SENS} v {COA, ENV, SENS, DECOL}	0.02 (0.01 , 0.02)
{CP, SENS} v CP	0.01 (0.01 , 0.02)
{COA, CP, SENS} v {CP, SENS}	0.03 (0.02 , 0.04)
{ENV, CP, SENS} v {CP, SENS}	0.04 (0.04 , 0.05)
{COA, ENV, CP, SENS} v {COA, CP, SENS}	0.03 (0.02 , 0.04)
{COA, ENV, CP, SENS} v {ENV, CP, SENS}	0.03 (0.02 , 0.04)
all v {COA, ENV, CP, SENS}	0.16 (0.15 , 0.18)

Supplementary Table S10: θ estimates for AR comparisons of intervention combinations for the high burden setting.

Comparison	AC $\hat{\theta}$ (95% CI)
COA v baseline	0.00 (0.00 , 0.00)
ENV v baseline	0.53 (0.51 , 0.56)
CP v baseline	0.61 (0.58 , 0.63)
SENS v baseline	0.86 (0.84 , 0.87)
DECOL v baseline	0.65 (0.63 , 0.67)
COA v ENV	0.00 (0.00 , 0.00)
COA v CP	0.00 (0.00 , 0.00)
COA v DECOL	0.00 (0.00 , 0.00)
COA v SENS	0.00 (0.00 , 0.00)
{COA, .} v {ENV, CP}	0.00 (0.00 , 0.00)
{COA, .} v {ENV, DECOL}	0.00 (0.00 , 0.00)
{COA, .} v {CP, DECOL}	0.00 (0.00 , 0.00)
{COA, .} v {ENV, SENS}	0.00 (0.00 , 0.00)
{COA, .} v {CP, SENS}	0.00 (0.00 , 0.00)
{COA, .} v {SENS, DECOL}	0.00 (0.00 , 0.00)
{COA, ., .} v {ENV, CP, DECOL}	0.00 (0.00 , 0.00)
{COA, ., .} v {ENV, CP, SENS}	0.00 (0.00 , 0.00)
{COA, ., .} v {ENV, SENS, DECOL}	0.00 (0.00 , 0.00)
{COA, ., .} v {CP, SENS, DECOL}	0.00 (0.00 , 0.00)
{COA, ., ., .} v {ENV, CP, SENS, DECOL}	0.00 (0.00 , 0.00)

Supplementary Table S11: θ estimates for AC comparisons of intervention combinations for high burden setting .

Comparison	C_d $\hat{\theta}$ (95% CI)
COA v baseline	0.14 (0.12 , 0.15)
ENV v baseline	0.36 (0.34 , 0.39)
CP v baseline	0.17 (0.15 , 0.19)
SENS v baseline	0.79 (0.76 , 0.80)
DECOL v baseline	0.62 (0.60 , 0.65)
COA v CP	0.45 (0.42 , 0.47)
COA v ENV	0.22 (0.20 , 0.24)
COA v DECOL	0.09 (0.08 , 0.10)
COA v SENS	0.03 (0.02 , 0.04)
CP v ENV	0.26 (0.24 , 0.28)
CP v DECOL	0.11 (0.10 , 0.13)
CP v SENS	0.04 (0.03 , 0.05)
{COA, CP} v {COA, ENV}	0.23 (0.21 , 0.25)
{COA, CP} v {ENV, CP}	0.13 (0.11 , 0.14)
{COA, CP} v {COA, SENS}	0.10 (0.09 , 0.12)
{COA, CP} v {COA, DECOL}	0.09 (0.08 , 0.10)
{COA, CP} v {CP, DECOL}	0.04 (0.04 , 0.05)
{COA, CP} v {CP, SENS}	0.01 (0.01 , 0.02)
{COA, CP} v {ENV, DECOL}	0.01 (0.01 , 0.02)
{COA, CP} v {ENV, SENS}	0.00 (0.00 , 0.01)
{COA, CP} v {SENS, DECOL}	0.00 (0.00 , 0.00)
{COA, ENV, CP} v {COA, CP, SENS}	0.30 (0.28 , 0.33)
{COA, ENV, CP} v {COA, CP, DECOL}	0.30 (0.27 , 0.32)
{COA, ENV, CP} v {COA, ENV, SENS}	0.16 (0.14 , 0.18)
{COA, ENV, CP} v {COA, ENV, DECOL}	0.11 (0.10 , 0.13)
{COA, ENV, CP} v {COA, SENS, DECOL}	0.06 (0.05 , 0.07)
{COA, ENV, CP} v {ENV, CP, DECOL}	0.03 (0.02 , 0.04)
{COA, ENV, CP} v {ENV, CP, SENS}	0.02 (0.01 , 0.02)
{COA, ENV, CP} v {CP, SENS, DECOL}	0.00 (0.00 , 0.01)
{COA, ENV, CP} v {ENV, SENS, DECOL}	0.00 (0.00 , 0.00)
{COA, ENV, CP, SENS} v {COA, ENV, CP, DECOL}	0.47 (0.45 , 0.50)
{COA, ENV, CP, SENS} v {COA, CP, SENS, DECOL}	0.31 (0.29 , 0.33)
{COA, ENV, CP, SENS} v {COA, ENV, SENS, DECOL}	0.18 (0.16 , 0.20)
{COA, ENV, CP, SENS} v {ENV, CP, SENS, DECOL}	0.01 (0.01 , 0.02)
{COA, ENV, CP, DECOL} v {COA, CP, SENS, DECOL}	0.33 (0.31 , 0.36)
{COA, ENV, CP, DECOL} v {COA, ENV, SENS, DECOL}	0.20 (0.18 , 0.22)
{COA, ENV, CP, DECOL} v {ENV, CP, SENS, DECOL}	0.01 (0.01 , 0.02)
{COA, CP} v COA	0.10 (0.09 , 0.11)
{COA, ENV, CP} v COA	0.03 (0.03 , 0.04)
{COA, ENV, CP} v {COA, CP}	0.28 (0.26 , 0.30)
{COA, ENV, CP, SENS} v {COA, CP}	0.23 (0.21 , 0.25)
{COA, ENV, CP, DECOL} v {COA, CP}	0.25 (0.23 , 0.27)
{COA, ENV, CP, SENS} v {COA, ENV, CP}	0.43 (0.41 , 0.46)
{COA, ENV, CP, DECOL} v {COA, ENV, CP}	0.46 (0.43 , 0.48)
all v {COA, CP}	0.16 (0.15 , 0.18)
all v {COA, ENV, CP}	0.35 (0.32 , 0.37)
all v {COA, ENV, CP, SENS}	0.42 (0.39 , 0.44)
all v {COA, ENV, CP, DECOL}	0.39 (0.37 , 0.41)

Supplementary Table S13: θ estimates for C_d comparisons of intervention combinations for high burden setting .

Comparison	I_{xd} $\hat{\theta}$ (95% CI)
COA v baseline	0.38 (0.36 , 0.41)
ENV v baseline	0.47 (0.44 , 0.49)
CP v baseline	0.40 (0.38 , 0.42)
SENS v baseline	0.00 (0.00 , 0.01)
DECOL v baseline	0.55 (0.52 , 0.57)
SENS v COA	0.02 (0.01 , 0.03)
SENS v CP	0.01 (0.01 , 0.02)
SENS v ENV	0.01 (0.00 , 0.01)
SENS v DECOL	0.00 (0.00 , 0.01)
{SENS, .} v {COA, CP}	0.04 (0.04 , 0.06)
{SENS, .} v {COA, ENV}	0.03 (0.02 , 0.03)
{SENS, .} v {ENV, CP}	0.02 (0.01 , 0.02)
{SENS, .} v {COA, DECOL}	0.02 (0.01 , 0.02)
{SENS, .} v {CP, DECOL}	0.01 (0.01 , 0.01)
{SENS, .} v {ENV, DECOL}	0.01 (0.00 , 0.01)
{SENS, ., .} v {COA, ENV, CP}	0.06 (0.05 , 0.08)
{SENS, ., .} v {COA, CP, DECOL}	0.05 (0.04 , 0.06)
{SENS, ., .} v {COA, ENV, DECOL}	0.03 (0.02 , 0.04)
{SENS, ., .} v {ENV, CP, DECOL}	0.01 (0.01 , 0.02)
{SENS, ., ., .} v {COA, ENV, CP, DECOL}	0.07 (0.06 , 0.08)

Supplementary Table S14: θ estimates for I_{xd} comparisons of intervention combinations for high burden setting .

Comparison	I_d $\hat{\theta}$ (95% CI)
COA v baseline	0.38 (0.36 , 0.41)
ENV v baseline	0.47 (0.44 , 0.49)
CP v baseline	0.40 (0.38 , 0.43)
SENS v baseline	0.00 (0.00 , 0.01)
DECOL v baseline	0.55 (0.52 , 0.57)
SENS v COA	0.02 (0.01 , 0.03)
SENS v CP	0.01 (0.01 , 0.02)
SENS v ENV	0.01 (0.00 , 0.01)
SENS v DECOL	0.00 (0.00 , 0.01)
{SENS, .} v {COA, CP}	0.05 (0.04 , 0.06)
{SENS, .} v {COA, ENV}	0.03 (0.02 , 0.03)
{SENS, .} v {ENV, CP}	0.01 (0.01 , 0.02)
{SENS, .} v {COA, DECOL}	0.02 (0.01 , 0.02)
{SENS, .} v {CP, DECOL}	0.01 (0.01 , 0.01)
{SENS, .} v {ENV, DECOL}	0.01 (0.00 , 0.01)
{SENS, ., .} v {COA, ENV, CP}	0.06 (0.05 , 0.08)
{SENS, ., .} v {COA, CP, DECOL}	0.05 (0.04 , 0.06)
{SENS, ., .} v {COA, ENV, DECOL}	0.03 (0.02 , 0.04)
{SENS, ., .} v {ENV, CP, DECOL}	0.01 (0.01 , 0.02)
{SENS, ., ., .} v {COA, ENV, CP, DECOL}	0.07 (0.06 , 0.08)

Supplementary Table S15: θ estimates for I_d comparisons of intervention combinations for high burden setting .

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