Introduction

The one-hospital model as presented here, allows us to characterize analytically (and next calculate numerically) the maximum R_0 value that can be reduced to ≤ 1 by a specified (combination of) intervention method(s). Furthermore, this model serves as an independent method to check the result of the simulation model in the main article.

Any R_0 calculation should be based on the situation when the infectious agent is hardly present and the infectivity of infectious individuals is not reduced because of waste of possible infectious contacts with individuals who are already infected. In this analysis we assume that methicillin-resistant *Staphylococcus aureus* (MRSA) is very rare.

Basic Model

Dynamics in a Single Unit. Pathogen dynamics within a hospital ward is generated by cross transmission and the discharge and admission of patients. Admission and discharge of patients happen at the same fixed time of the day and newly admitted patients are not colonized, i.e., the outbreak is triggered by just one exceptional case. We will describe a new colonization resulting from transmission as an "acquisition" and, accordingly, talk about the number of acquisitions during a day.

Let $P(y|x)$ be the probability that y patients in the unit are colonized at time $t+1$ just before discharge and admission, given that x colonized patients were present in the unit at time t just after discharge and admission. Assuming that uncolonized patients can acquire colonization only from those patients who were already colonized after admission and discharge and not in a two-step procedure during one and the same day, $P(y|x)$ is binomially distributed, i.e.,

$$P(y|x) = \begin{cases} 0 & \text{if } y < x \\ \binom{N-x}{y-x}\left(1-e^{\frac{-\beta x}{N-1}}\right)^{y-x}\left(e^{\frac{-\beta x}{N-1}}\right)^{N-y} & \text{if } y \geq x \end{cases} \qquad [1]$$

with β the transmission parameter. When $\frac{\beta}{N-1}$ is small, the expected number of acquisitions in the first day after admission of a primary case to a "virgin" ward is independent of the size of the ward and equal to β.

Length of stay is independent of colonization geometrically distributed with discharge rate

$\frac{1}{d}$. Colonization persists during the stay in the unit. The probability $\hat{P}(z|y)$ that there are z colonized patients after discharge and admission, given that there were y colonized patients in the unit before discharge and admission, is given by ($0 \leq y, z \leq N$):

$$\hat{P}(z|y) = \begin{cases} 0 & \text{if } z > y \\ \binom{y}{z} \left(\frac{1}{d}\right)^{y-z} \left(1 - \frac{1}{d}\right)^{z} & \text{if } z \leq y \end{cases} \quad [2]$$

The transition probabilities $f(b|a)$ that there are b colonized patients in the unit directly after discharge and admission at time $t+1$, given there were a colonized patients in the unit directly after discharge and admission at time t, and the expected number of acquisitions of colonization $g(b|a)$ in a transition from a to b colonized patients are given by:

$$f(b|a) = \sum_{j=0}^{N-a} P(a+j|a)\hat{P}(b|a+j) \quad [3]$$

$$g(a,b) = \frac{\sum_{j=0}^{N-a} jP(a+j|a)\hat{P}(b|a+j)}{f(b|a)} \quad [4]$$

Let $E(k)$ be the expected total number of new acquisitions in the unit when there are k colonized patients in the unit directly after admission and discharge. By definition,

$$E(0) = 0 \quad [5]$$

If there are k colonized patients in the unit, 1 day later there will be b ($0 \leq b \leq N$) colonized patients in the unit with probability $f(k|b)$. During the transition from k to b colonized patients, $g(k,b)$ will have become colonized. By definition, after this day, on average $E(k)$ will become colonized in the unit. Hence we have the following relation for $E(k)$:

$$E(k) = \sum_{b=0}^{N} f(b|k)\left(E(b) + g(k,b)\right) \qquad 1 \leq k \leq N \quad [6]$$

A Hospital With Many Units. After admission of a colonized patient, the first acquisition occurs with probability p in the same unit. We want to specify the ratio between secondary

cases in the own ward and in other wards, while bypassing the effect of a strong reduction in available susceptibles in the own ward. If the ratio is $p : 1-p$ and the number of secondary cases in the own ward after 1 day equals β, we expect $\frac{1-p}{p}\beta$ secondary cases in other units after 1 day.

With an infinite number of wards, all patients in other wards infected by patients in the initial ward will be in different wards with probability 1. The expected size of the total outbreak T (excluding the index case) satisfies a consistency relation **[7]** which leads to **[8]**, provided this expression is positive (1). The outbreak size T consists of the number of acquisitions in the unit of the index case ($E(1)$). Next, we want to calculate the number of acquisitions outside the initial unit. Therefore we calculate the expected number of days during which the colonized patients in the initial unit were able to spread. As the average length of stay is d days, the index case spreads for an average of d days. Because we assumed that uncolonized patients can acquire colonization only from those patients who were already colonized after admission and discharge and not in a two-step procedure during one and the same day, the patients who acquired colonization in the initial ward can only transmit to other units if they are not discharged on the day directly following acquisition (probability $1/d$). Hence the expected total number of days during which patients in the initial unit are capable to spread to other units is $d(1 + \frac{d-1}{d}E(1))$. Per day, a colonized patients infects on average $\frac{1-p}{p}\beta$ patients in other units. Hence the expected total number of cases of transmission from patients in the initial ward to patients in other wards is $\frac{(1-p)}{p}\beta d(1+\frac{d-1}{d}E(1))$. As we assumed that the number of wards is infinite, each of these acquisitions will be in a different ward. If these patients are not discharged the day directly following acquisition (probability $1/d$), these patients will generate each on average T new cases.

$$T = E(1) + \frac{(1-p)}{p}\beta d(1 + \frac{d-1}{d}E(1))(1 + \frac{d-1}{d}T) \quad [7]$$

$$T = \frac{pE(1) + (1-p)\beta d(1 + \frac{d-1}{d}E(1))}{p - (1-p)\beta(d-1)(1 + \frac{d-1}{d}E(1))} \quad [8]$$

With a finite number of wards, all acquisitions outside the initial ward need not occur in "virgin" wards. T can be regarded as a worst case scenario, as the expected number of transmissions for a patient is maximal when all other patients within the unit are susceptible. When ward size goes to infinity, the outbreak size satisfies $T = \beta d/(p - \beta(d-1))$ (1).

Readmission. When $T < \infty$, readmission of colonized patients is essential for persistence. Let ξ be the probability that a patient leaving the hospital while being colonized will reenter the hospital at some later time while still being a carrier. Deaths are immediately replaced by uncolonized individuals, and the probability that an individual dies while still being colonized can be incorporated in ξ. To persist in the community (both extramural and intramural), the expected size of an outbreak T should exceed the critical value T_c, defined by:

$$(1 + T_c)\xi = 1. \qquad [9]$$

As T depends (possibly in a complicated way) on other parameters, one can use $T_c = \frac{1}{\xi} - 1$ to define a critical value of one of these (by fixing the value of all the other parameters). In a hospital with wards of infinite size, the critical value for β is given by: $\beta_c = (p(1-\xi))/(d-1+\xi)$. With wards of smaller size, the recursion **[6]** has to be solved after which **[8]** and **[9]** can be used. As the pool of susceptibles declines faster in small units, reduction in unit size in itself reduces transmission.

Interventions. ***Isolation of identified carriers (measure I)*** Patients colonized with MRSA are detected as carriers by clinical cultures with probability ν per day. All cultures are performed at the same moment of the day, immediately before the moment of discharge and admission. For modeling purposes, we assume that culture results are available at once and are 100% reliable. Patients remain in isolation till discharge and, therefore, no longer spread MRSA to other patients. From a modeling perspective, we can consider isolated patients as effectively discharged while making sure that this does not influence the number of unisolated patients. The effective discharge probability per day for a colonized patient then becomes $(1 + (d - 1)\nu)/d$. Although the discharge probability for uncolonized patients remains $1/d$, for technical simplicity we can assume it to be $(1 + (d-1)\nu)/d$ as well, as the replacement of an uncolonized patient by another uncolonized patient has no effect. For a ward of infinite size, the relative increase in the critical transmission parameter will be $1 + (d-1)\nu$ (provided the isolation capacity is sufficiently large). For a hospital consisting of wards of finite size, equations **[6]**, **[8]** and **[9]** have to be solved in

which d should be replaced by $d/(1+(d-1)\nu)$.

Isolation and screening of contact patients (measures I+III). When at least one colonized patient is identified, all other patients in the unit will be screened, and colonization will be detected with probability θ per carrier. In this case the "discharge" function should cover both the situation with and without detection of colonization of (at least) one colonized patient. Suppose there are y colonized patients in the unit. If colonization is detected in none of the y colonized patients (probability $(1-\nu)^y$), we obtain the old discharge function **[2]**. If colonization is detected in at least one patient (let j be the number of detected colonized patients), these patients will be isolated (and removed from the unit), and the remaining patients will be screened. Colonization in colonized patients is detected with probability θ. (False positive patients are of no concern in this setting. We assume isolation capacity is always sufficient and for the transmission process false positive patients are not important as these patients would be removed from the unit, and the empty bed would immediately be occupied by new patients which are assumed to be uncolonized.) When patients within the unit are screened for colonization, colonized patients can leave the unit in two ways. Either they are discharged (probability $1/d$) or, if they are not discharged (probability $1-1/d$), colonization is detected, after which they are isolated.

$$\hat{P}(z|y) = \begin{cases} 0 \text{ if } z > y \\ \binom{y}{z}(1-\nu)^y \left(\frac{1}{d}\right)^{y-z}\left(1-\frac{1}{d}\right)^z + \sum_{j=1}^{y-z}\binom{y}{j}(1-\nu)^{y-j}\nu^j \\ \binom{y-j}{z}\left(\frac{1+(d-1)\theta}{d}\right)^{y-j-z}\left(\frac{d-1}{d}(1-\theta)\right)^z \text{ if } 0 \le z \le y \end{cases} \quad [10]$$

When $\theta = 1$, all colonized patients are transferred to isolation rooms, all remaining patients will be uncolonized, and the discharge function simplifies to:

$$\hat{P}(z|y) = \begin{cases} 0 & \text{if } z > y \\ \binom{y}{z}\left(\frac{1}{d}\right)^{y-z}\left(1-\frac{1}{d}\right)^z(1-\nu)^y & \text{if } 0 < z \le y \\ (1-\nu)^y\left(\frac{1}{d}\right)^y + (1-(1-\nu)^y) & \text{if } z = 0 \end{cases} \quad [11]$$

Using **[3]** and **[4]** with the new "discharge" function and **[6]**, **[8]** and **[9]**, the new critical value

of the transmission parameter can be calculated.

Isolation and screening of high-risk patients (measures I+II). Let S be the expected number of colonized patients, per outbreak in the hospital as a whole, who were identified as MRSA carriers during hospitalization (including the index patient). S satisfies the relation:

$$S = \frac{\nu}{\nu + (1-\nu)\frac{1}{d}}(1+T) \qquad [12]$$

as each colonized patient has a probability $\frac{\nu}{\nu+(1-\nu)\frac{1}{d}}$ to be detected. Note that T should be calculated using an effective discharge probability of $\frac{1+(d-1)\nu}{d}$. When a fraction $1-g$ of the previously colonized patients is missed by the screening, we find the following relation for criticality:

$$(1+T-S)\xi + S\frac{\xi(1-g)}{1-\xi g} = 1 \qquad [13]$$

(The last term comes from the geometric series: Of the S patients, a fraction $(\xi g)^{j-1}\xi(1-g)$ will be able to spread at the j^{th} admission and could not spread at any previous admissions.)

The "Search & Destroy" policy (measures I+II+III). Due to the screening of contact patients, the probability to detect colonization depends on the total number of colonized patients in the unit. Let $S(k)$ be the expected number of detected cases in an outbreak in a single ward when the outbreak starts with k (undetected) patients. Let $h(x,y)$ denote the expected number of detected patients in a transition from x colonized patients to y colonized patients. If we condition on the transition in the number of patients during the first day, we see that the $S(k)$ satisfy the following set of linear equations:

$$\begin{aligned} S(0) &= 0 \\ S(k) &= \sum_{b=0}^{N} f(b|k)\,(S(b) + h(k,b)) \end{aligned} \qquad [14]$$

where we should use equation **[10]** in the definition of the transition probability f **[3]**. $h(x,y)$ is given by equation **[15]**. If there are initially x (undetected) colonized patients in the unit, due to transmission **[1]**, 1 day later there will be $x+j$ ($0 \le j \le N-x$) colonized patients in the unit with probability $P(x+j|x)$. Colonization is detected by clinical cultures in i ($0 \le i \le x+j$) of

these $x+j$ positive patients with probability $\binom{x+j}{i}(1-\nu)^{x+j-i}\nu^i$. To have y undetected colonized patients remaining after the screening and discharge of the patients in the unit, $x+j-i-y$ of the $x+j-i$ undetected colonized patients should either be discharged or their colonization should be detected by the screening. The probability of this event is $\binom{x+j-i}{y}\left(\frac{1+(d-1)\theta}{d}\right)^{x+j-i-y}\left(\frac{d-1}{d}(1-\theta)\right)^y$. As the probability that colonization is actually detected in one of the $x+j-i-y$ patients is $\frac{\theta}{\theta+(1-\theta)\frac{1}{d}}$, the expected number of detected patients during this day is $\left(i+\frac{\theta}{\theta+(1-\theta)\frac{1}{d}}(x+j-i-y)\right)$. By summing over all possible transitions and by dividing by $f(y|x)$ to normalize the expression, we obtain the following expression for $h(x,y)$.

$$\begin{aligned} h(x,y) = \tfrac{1}{f(y|x)} \sum_{j=0}^{N-x} \sum_{i=1}^{x+j-y} P(x+j|x)\tbinom{x+j}{i}(1-\nu)^{x+j-i}\nu^i\tbinom{x+j-i}{y} \\ \left(\tfrac{1+(d-1)\theta}{d}\right)^{x+j-i-y}\left(\tfrac{d-1}{d}(1-\theta)\right)^y \left(i+\tfrac{\theta}{\theta+(1-\theta)\frac{1}{d}}(x+j-i-y)\right) \end{aligned} \quad [15]$$

(Note that when $i=0$, no colonization will be detected and these terms do not contribute to the expectation.) When the screening will reveal every colonized patient ($\theta=1$), equation **[14]** simplifies to:

$$\begin{aligned} S(0) &= 0 \\ S(k) &= \sum_{b=1}^{N} f(b|k)S(b) + \sum_{j=0}^{N-k} P(k+j|k)(k+j)\left\{1-(1-\nu)^{k+j}\right\} \end{aligned} \quad [16]$$

where we can use **[11]** to determine the transition probabilities **[3]**.

Let $D(k)$ be the severity of the outbreak within a unit, given that there are initially k infectious patients in the ward, i.e., the total number of patient days during which the patients were colonized before the natural fade out of the outbreak or the detection of the outbreak. If we condition on the transition in the number of patients during the first day, we see that the $D(k)$ satisfy the following set of linear equations:

$$\begin{aligned} D(0) &= 0 \\ D(k) &= k + \sum_{b=0}^{N} f(b|k)D(b) \end{aligned} \quad [17]$$

The expected total number T of patients infected during an outbreak (which may spread over several wards) and the total number S of detected patients satisfy the equations which can

be derived in a similar way as equation **[7]**:

$$\begin{aligned} T &= E(1) + \tfrac{(1-p)}{p}\beta D(1)(1 + \tfrac{d-1}{d}T) \\ S &= S(1) + \tfrac{(1-p)}{p}\beta D(1)(\nu + (1-\nu)\tfrac{d-1}{d}S) \end{aligned} \qquad [18]$$

With these results, **[18]** and the relation **[13]**, we can determine the effect of the "search & destroy" policy.

Active decolonization (measures I+II+III+VI). Suppose colonization is successfully eradicated in a fraction ϕ of patients. This can be incorporated in the condition for criticality. The total number S' of detected patients for which decolonization was unsuccessful satisfies

$$S' = S(1-\phi) \qquad [19]$$

while the expected total number T' of patients infected during an outbreak and not successfully decolonized is given by:

$$T' = T - \phi S \qquad [20]$$

These expressions can be used in the relation for criticality **[13]** in which we also assume that when colonization has failed and these patients are recognized as risk patients upon readmission, active decolonization is tried again with the same probability of success. This leads to:

$$\begin{gathered} (1 + (T - \phi S) - (1-\phi)S)\,\xi + S\tfrac{\xi(1-\phi)(1-g)}{1-\xi(1-\phi)g} = 1 \Rightarrow \\ (1 + T - S)\,\xi + S\tfrac{\xi(1-\phi)(1-g)}{1-\xi(1-\phi)g} = 1 \end{gathered} \qquad [21]$$

A Core Group

The same analysis can be performed while including a core group with a different hospitalization rate. The remainder of this paper is devoted to deriving similar expressions for this more complicated case as obtained above for the homogeneous case.

For the model with a core group, we calculate the largest eigenvalue of a next-generation matrix. This eigenvalue (λ_{max}) can be seen as the reproduction ratio of outbreaks in a hospital

(1), and the relation $\lambda_{\max} = 1$ is the equivalent of the criticality condition **[9]**.

Background. In reality there is heterogeneity among individuals in the frequency of admission. Some individuals visit the hospital often, for example elderly. To take heterogeneity to some extent into account, we repeat the analysis of the previous section for two types of individuals (core group, noncore group) which differ only in their probability to be still colonized with MRSA when readmitted. Individuals from the core group are hospitalized more frequently. If the spontaneous decolonization rate is the same for the core and the noncore group or if the decolonization rate is smaller for the core group, the probability to be colonized upon readmission is higher for the core group. As the expected size of an outbreak within the hospital is not altered by the introduction of two types of patients with identical behaviour within the hospital, the calculation of the outbreak size T is identical to the situation without a core group. (Use **[3]**, **[4]**, **[6]**, **[8]** and **[10]**, **[11]** or **[2]** depending on whether there is an active search policy among contact patients of the index-patients or not, respectively.) However, the critical outbreak size T_c will change. A core group will enhance the importance of readmission and, therefore, a lower R_A can lead to persistence in the population (both intramural and extramural). As for a lower R_A, the average size of an outbreak will be smaller, and the depletion of the number of susceptibles will also be smaller. Therefore, the effects of the compartmental structure of the hospital on the critical transmission parameter will be smaller in case of a core group. Moreover, relative effects of elements of the "search & destroy" policy will be different.

Let ξ_i be the probability that a colonized patient of type i is still colonized when readmitted and let γ be the expected fraction of hospitalized patients of type 1. When all other characteristics of the two types of patients are identical and previously colonized patients are not screened when readmitted to the hospital, the pathogen can persist if and only if the largest eigenvalue of the next-generation matrix

$$\begin{pmatrix} (\gamma T + 1)\xi_1 & \gamma T \xi_1 \\ (1-\gamma) T \xi_2 & ((1-\gamma)T + 1)\xi_2 \end{pmatrix} \qquad [22]$$

exceeds 1. The largest eigenvalue is equal to 1 when the outbreak size T equals:

$$T_c = \frac{(1-\xi_1)(1-\xi_2)}{\xi_2(1-\xi_1)+\gamma(\xi_1-\xi_2)} \qquad [23]$$

The largest eigenvalue can be seen as the reproduction ratio of outbreaks in a hospital.

Isolation of identified carriers (measure I). We will now investigate the effect of different intervention measures in the presence of a core group. If the only intervention is to isolate patients known to be colonized with MRSA by clinical cultures, **[23]** still applies, but T should be determined using an effective length of stay of $\frac{d}{1+(d-1)\nu}$ in **[2]** and **[8]**, see *Isolation of identified carriers* in *Interventions* within the *Basic Model*.

Isolation and screening of contact patients (measures I+III). See *"search & destroy" policy (measures I+II+III)* with $g = 0$.

Isolation and screening of high-risk patients (measures I+II). Now, screening of patients, known to be colonized during previous hospitalization with efficacy g, is added. Without additional screening of contact patients in case of an unexpected case of MRSA colonization, each colonized patient has a probability to be detected of $\frac{\nu}{\nu+(1-\nu)\frac{1}{d}}$. Let $\eta(\nu, d, g, \xi_i)$ be the probability that a patient of type i who acquires colonization during hospitalization will ever return to the hospital while still being colonized but without being notified as such. When colonization was not detected during hospitalization (probability $1-\frac{\nu}{\nu+(1-\nu)\frac{1}{d}}$), the patient is still colonized at the next admission with probability ξ_i. When colonization was detected during hospitalization, the patient has a probability $\xi^m g^{m-1}(1-g)$ to be able to transmit during the m^{th} admission without the ability to spread at any of the previous admissions. Therefore we have that:

$$\eta(\nu, d, g, \xi) = \xi\left(1 - \frac{\nu}{\nu+(1-\nu)\frac{1}{d}} + \frac{\nu}{\nu+(1-\nu)\frac{1}{d}}\frac{1-g}{1-\xi g}\right) \qquad [24]$$

Note that $\eta(\nu, d, g, \xi) = \xi$ when the efficacy g of screening on admission of high-risk patients is

0. The next generation matrix is given by:

$$\begin{pmatrix} (\gamma T+1)\eta(\nu,d,g,\xi_1) & \gamma T\eta(\nu,d,g,\xi_1) \\ (1-\gamma)T\eta(\nu,d,g,\xi_2) & ((1-\gamma)T+1)\,\eta(\nu,d,g,\xi_2) \end{pmatrix} \quad [25]$$

where T again should be determined using an effective length of stay of $\frac{d}{1+(d-1)\nu}$. The pathogen can persist if and only if the largest eigenvalue of the next generation matrix exceeds 1.

The "Search & Destroy" policy (measures I+II+III). With active search for MRSA among contact patients after an unexpected identification of colonization with MRSA upon clinical cultures and screening on admission of previously colonized patients with efficacy g, the calculation is less straightforward as the number of detected patients of type i depends on whether the initial colonized patient was of type i or not. As the typical size of an outbreak is small, the type of the initial patient cannot be neglected. Let $Q(k)$ denote the probability that colonization of the index patient is detected, given that there are k colonized patients in the unit (including the index patient) at the start of that day. We first consider the case when screening detects all colonized patients in the unit ($\theta = 1$). Suppose that during that day j uncolonized patients in the unit acquire colonization. If the colonization of at least one of the $k+j$ colonized patients is detected (probability $1-(1-\nu)^{k+j}$), all patients in the unit will be screened and the colonization of the index patient is also detected. If colonization of none of the $k+j$ patients is detected by clinical cultures, colonization of the index patient can only be detected if the index patient is not discharged and the probability of detection will depend on the number of colonized patients that remain in the unit. Therefore, the $Q(k)$ satisfy the following relations for $1 \leq k \leq N$:

$$\begin{aligned} Q(k) = \sum_{j=0}^{N-k} P(k,k+j)\left(1-(1-\nu)^{j+k}\right) + \\ \sum_{j=0}^{N-k} P(k,k+j)(1-\nu)^{j+k} \sum_{z=1}^{j+k} \binom{j+k}{z} \left(\tfrac{1}{d}\right)^{(j+k-z)} \left(1-\tfrac{1}{d}\right)^{z} \tfrac{z}{j+k} Q(z) \end{aligned} \quad [26]$$

where the term $\frac{z}{j+k}$ represents the probability that the index patient was not among the discharged colonized patients.

When $\theta \neq 1$, the expression becomes more complicated. We again condition on the number of acquisitions (j) during the first day. After that, we distinguish between two cases. The first

summation in **[27]** deals with the case when colonization is detected by clinical cultures in none of the colonized patients (probability $(1-\nu)^{k+j}$)). This case is comparable with the situation when $\theta = 1$. The double summation of **[27]** deals with the case that colonization is detected by way of clinical cultures in at least one of the colonized patients. The probability that colonization is detected by clinical cultures in i patients is $\begin{pmatrix} k+j \\ i \end{pmatrix} (1-\nu)^{k+j-i}\nu^i$. We next sum over the remaining number of colonized patients (z) after screening and discharge. The probability that there are z remaining colonized patients is $\begin{pmatrix} k+j-i \\ z \end{pmatrix} \left(\frac{1+(d-1)\theta}{d}\right)^{k+j-i-z} \left(\frac{d-1}{d}(1-\theta)\right)^z$. The probability that colonization will be detected in the index patients can be divided over three cases.

1. Colonization in the index patient was found by a clinical culture (probability $i/(k+j)$);
2. Colonization was not found by a clinical culture but due to the screening (probability $\frac{k+j-i-z}{k+j}\frac{\theta}{\theta+(1-\theta)\frac{1}{d}}$); and
3. Colonization is not detected in the index patient during that day but the index patient is still in the unit and colonization will be detected later on (probability $\frac{z}{k+j}Q(z)$).

This leads to the following linear set of equations for $Q(k)$:

$$
\begin{aligned}
Q(k) = \sum_{j=0}^{N-k} P(k,k+j) \\
\left(\sum_{z=0}^{k+j} \begin{pmatrix} k+j \\ z \end{pmatrix} (1-\nu)^{k+j} \left(\tfrac{1}{d}\right)^{k+j-z} \left(1-\tfrac{1}{d}\right)^z \tfrac{z}{k+j} Q(z) + \right. \\
\sum_{z=0}^{k+j} \sum_{i=1}^{k+j} \begin{pmatrix} k+j \\ i \end{pmatrix} (1-\nu)^{k+j-i}\nu^i \begin{pmatrix} k+j-i \\ z \end{pmatrix} \left(\tfrac{1+(d-1)\theta}{d}\right)^{k+j-i-z} \\
\left. \left(\tfrac{d-1}{d}(1-\theta)\right)^z \tfrac{1}{k+j} \left\{ i + (k+j-i-z)\tfrac{\theta}{\theta+(1-\theta)\frac{1}{d}} + zQ(z) \right\} \right)
\end{aligned}
\qquad [27]
$$

Let T_{ij} denote the expected number of new cases of type j when the initial case was of type i and let S_{ij} denote the expected number of detected cases of type j when the initial case was of type i. We obtain as next generation matrix:

$$
\begin{pmatrix}
\xi_1(1+T_{11}-S_{11})+S_{11}\frac{\xi_1(1-g)}{1-\xi_1 g} & \xi_1(T_{21}-S_{21})+S_{21}\frac{\xi_1(1-g)}{1-\xi_1 g} \\
\xi_2(T_{12}-S_{12})+S_{12}\frac{\xi_2(1-g)}{1-\xi_2 g} & \xi_2(1+T_{22}-S_{22})+S_{22}\frac{\xi_2(1-g)}{1-\xi_2 g}
\end{pmatrix}
\qquad [28]
$$

The pathogen can persist if and only if the largest eigenvalue of this matrix exceeds 1.

The calculation of T_{ij} is easy, as T is defined as the expected size of an outbreak excluding the index patient. Therefore, on average, a fraction γ of T patients will be of type 1 and a fraction $(1-\gamma)$ of type 2. The calculation of S_{ij} is more complex, as S is defined as the expected number of colonized patients for which colonization is detected. Therefore, index patients also contribute to S, and we have to use the probability $Q(1)$ that colonization is detected in the index patient. We obtain:

$$\begin{aligned} T_{i1} &= \gamma T \qquad & i \in \{1,2\} \\ T_{i2} &= (1-\gamma)T \qquad & i \in \{1,2\} \\ S_{11} &= \gamma S + (1-\gamma)Q(1) \\ S_{12} &= (1-\gamma)(S - Q(1)) \\ S_{21} &= \gamma S - \gamma Q(1) \\ S_{22} &= (1-\gamma)S + \gamma Q(1) \end{aligned} \qquad [29]$$

Active decolonization (measures I+II+III+VI). When colonized patients of type i treated in isolation rooms are actively decolonized with efficacy ϕ_i, the relations for T_{ij} and S_{ij} in system **[29]** change. The new values (denoted with a prime) are given by:

$$\begin{aligned} S'_{ij} &= S_{ij}(1-\phi_j) \\ T'_{ij} &= T_{ij} - S_{ij}\phi_j \end{aligned} \qquad [30]$$

The effects of different prevention strategies are shown in Figure 4 and 10. Note that the calculation in this section can be extended to a situation with several core groups, each with a different readmission rate.

References

1. Bootsma, M. C. J. (2005) Ph.D. thesis (Utrecht Univ., Utrecht, The Netherlands).

Additional Figures

With the exception of Fig.10, the figures presented in this supplement are not results of the analytical model as described in the appendix but results of the simulation model as described in the main text.