Quantifying the transmission dynamics of MRSA in the community and healthcare settings in a low-prevalence country

Supplementary material

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1 Methods

1.1 Model structure

We studied the transmission of methicillin-resistant *Staphylococcus aureus* (MRSA) in Norway by developing a stochastic individual-based model with realistic socio-demographic characteristics and spatial information. The model includes approximately 5 million persons and simulates their social interactions in households, workplaces, schools and healthcare settings to reproduce the transmission dynamics of MRSA among humans. By including specific individual features of the population the model is able to capture heterogeneities in the routes of transmission and to characterize the main determinants of the MRSA epidemiology. Specifically, each individual in the model is characterized by the following characteristics:

- age (with a minimum of 0 and a maximum of 100 years);
- ethnic background (Norwegian or foreign-born background);
- type of occupation (student, teacher, generic worker, healthcare worker or unemployed);
- hospitalization status (not hospitalized, hospitalized, hospitalized in ICU or long-term nursing home resident);
- epidemiological status (susceptible, colonized or infected).

The synthetic population is distributed on a grid of 4978 cells (each covering an area of ~ 65 km^2) with specific geographic coordinates, representing the Norwegian territory. The population density in each cell reflects the real distribution of inhabitants in that specific area, obtained from the dataset of the Gridded Population of the World version 3 (GPW v3) produced by the Center for International Earth Science Information Network (CIESIN) of the Earth Institute at Columbia University.

1.1.1 Community setting

The individuals constituting the synthetic population live in households of different size and based on their age are associated to schools and workplaces. These settings represent the community environment of the model.

The construction of a realistic community setting has been performed adopting the procedure used in previous publications and described in detail in [1]. Individuals based on their age are assigned to different work places or schools (the model includes four school categories, from kindergartens to higher education institutions) following the observed distribution of the number of active and inactive individuals, obtained from Eurostat [2]. The association of each person to specific schools and workplaces distributed on the grid was carried out considering the average travel distance of individuals, which in previous studies was found to be well approximated by a truncated power law distribution [3]:

$$f(r) = (r + r_0)^{-\beta_r} e^{-\frac{r_0}{k}} \tag{1}$$

where, $r_0 = 5.8$ km, $\beta_r = 1.65$ and $k = 350$ km.

1.1.2 Healthcare setting

The model includes healthcare environments represented by hospitals and nursing-homes. A total of 58 hospitals are included in the model [4]. Each hospital is divided in wards whose size is sampled from a Gaussian distribution, with mean and standard deviation equal to 25 and 5, respectively [5]. For large hospitals we included intensive care units (ICUs), considering that on average there is an ICU every 300 beds [6].

Nursing-homes are generated knowing that in Norway the total number of beds occupied by long-term patients is approximately 1% of the total population [7]. The number of beds in each institution ranged between 20 and 152 beds [8]. The number of healthcare workers was set to respect a nurse-to-bed ratio of 0.2 (for hospitals [9]) and 0.3 (for nursing-homes [10]).

At any time step, individuals have a certain age-specific probability of being hospitalized, ranging from $3 \cdot 10^{-4}$ per day, in the age-group 0-39, to $2 \cdot 10^{-3}$ per day, in the age-group 80+.

The length of stay (LOS) is sampled from age-specific exponential distributions whose parameters were estimated by fitting the available data with information on the LOS of hospitalized patients in South-Eastern Norway (Fig. S1). The model does not consider movements of patients between wards in hospitals. This assumption is backed by data on patient movements in the South-Eastern region of Norway. In particular, our analyses showed that 91.2% of the inpatients were never transferred during a hospital stay, 7.2% were transferred to only one ward, 1.3% visited three wards and less than 0.2% moved between more than three wards.

Specific control measures, including screening activities, isolation procedures, work restrictions and decolonization therapies, have been implemented in healthcare institutions, as described in the Norwegian national MRSA surveillance document [11] .

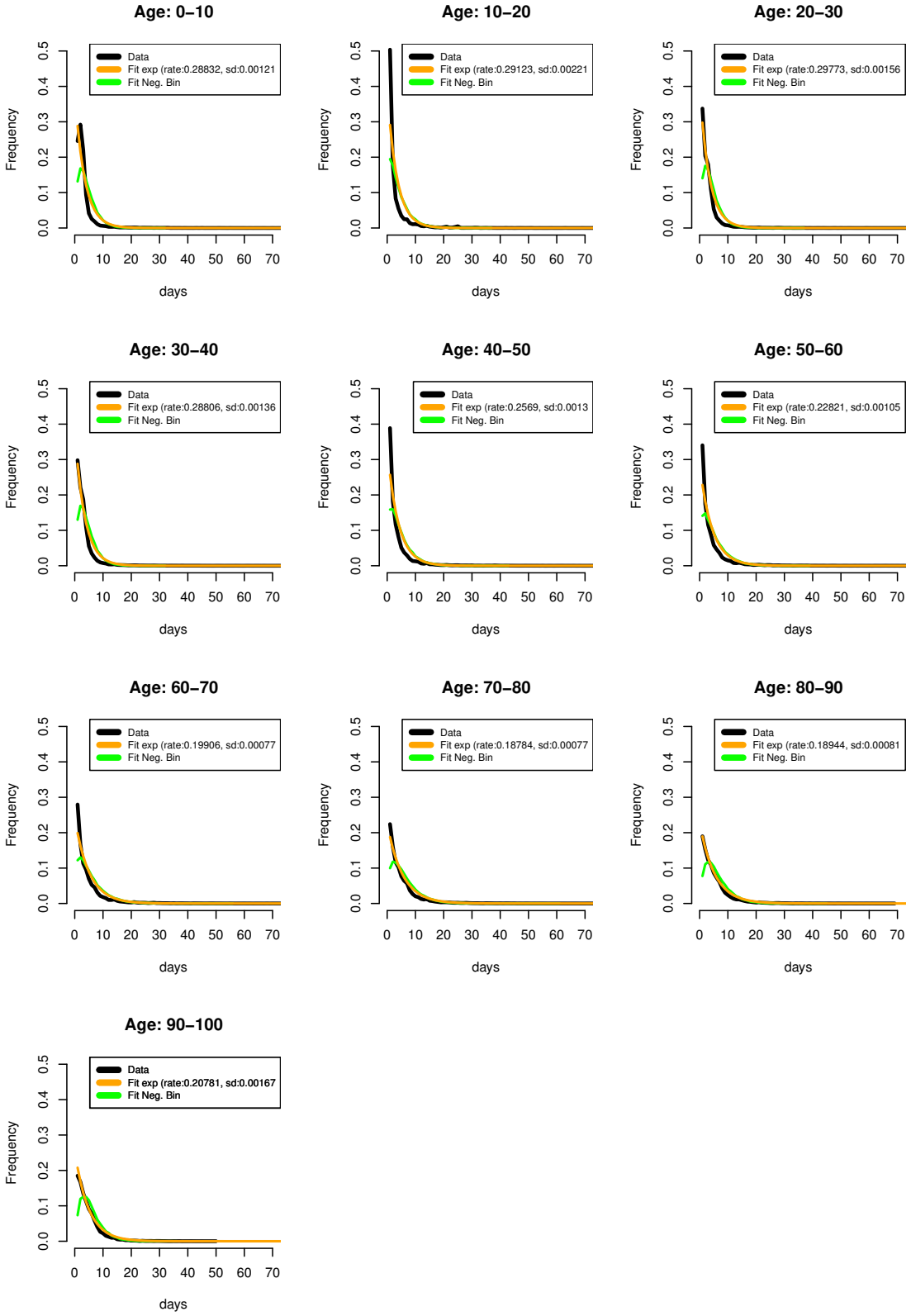


Figure S1: Distribution of patients' length of stay in hospital by age. For each age group, the data and the fitted distributions are represented (negative binomial and exponential).

1.2 Transmission model

Transmission of MRSA among persons occurs primarily by physical contacts. In our model, individuals are characterized by three possible disease states: Susceptible (S), Colonized (C) and Infected (I). Susceptible individuals can be infected by colonized or infected persons. When they acquire the bacterium, they firstly become colonized (asymptomatic carriers); colonized persons may either return to the susceptible state, by treatment or natural decolonization, or they can develop an infection with a progression rate that depends on the setting where the person is at time t, namely community, hospital, ICU or nursing home. The rate of infection is set from literature estimates in ICUs [12], hospitals [12], and nursing-homes [13]; in absence of reliable estimates for for the community, we let the progression rate in this setting as a free parameter.
Similarly, transmission rates β are setting-dependent. Individuals may become colonized in households, schools, workplaces, hospitals and nursing-homes, and from distance-dependent random contacts in the general population.

For the i-th individual the probability of becoming colonized is described by the following formula

$$p_i = 1 - e^{-\Delta t \cdot \lambda_i(t)} \tag{2}$$

where the force of infection, $\lambda_i(t)$, computed at each time step Δt, represents the risk of colonization and depends on the place where the i-th individual is at time t and hence on the number of persons that he could contact at these places. In the community the force of infections is defined as

$$\lambda_i = \sum_{k \in H_i} \frac{I_k \beta_h}{n(H_i)} + \sum_{k \in W_i} \frac{I_k \beta_w}{n(W_i)} + \sum_{k \in N} \frac{I_k \beta_r f(r_{ik})}{\sum_{k \in N} f(r_{ik})} \tag{3}$$

where:

- $I_k = 1$ if the individual is colonized or infected and $I_k = 0$ otherwise;
- β_h is the rate of colonization in households and $n(H_i)$ the number of persons in the same household of the i-th individual, H_i;
- β_w is the rate of colonization in schools/workplaces and $n(W_i)$ the number of persons in the same workplace of the i-th individual, W_i;
- β_r is the rate of colonization from random contacts in the general population;
- $f(r_{ik})$ represents the distribution of human mobility (eq. 1) and r_{ik} is the distance between the i-th individual and k-th individual in the total population, N.

For persons living and working in nursing homes, the force of infection is expressed as

$$\lambda_i = \sum_{k \in Q_i} \frac{I_k \beta_{nh}}{n(Q_i)} \tag{4}$$

where β_{nh} is the transmission rate in nursing homes and $n(Q_i)$ the number of patients and healthcare workers in the same nursing home of the i-th individual, Q_i.

When persons are hospitalized the force of infection assumes the following form,

$$\lambda_i = \sum_{k \in P_i} \frac{I_k \beta_{hosp}}{n(P_i)} \tag{5}$$

where, β_{hosp} is the rate of colonization in hospital and $n(P_i)$ the number of patients and healthcare workers in the same hospital ward of the i-th individual P_i.

For healthcare workers the force of infection takes the form described in eq. 3, with the term in equation 4 or 5 (depending on where they work) replacing the term of transmission in schools/workplaces ($\sum_{k \in W_i} \frac{I_k \beta_w}{n(W_i)}$).

At any time step, Δt, susceptible individuals in the community may also acquire MRSA via international travel. The number of persons positive to MRSA is characterized by a Poisson distribution with mean μ depending on age, ethnic-background and time. The stochastic importation process was calibrated on the data from the National Registry, where several information are reported for each case, such as ethnic background, age or the place of MRSA acquisition (Norway

or abroad) [14]. Parameters μ were estimated by fitting the monthly time series of the number of infected cases notified as acquired abroad in the national registry data, stratified by age-group (0-19, 20-39, 40-69, 70+ years old) and ethnic background (Norwegian vs. immigrant background) of the infected persons (Table S1). The category immigrant background includes all the persons born abroad or having parents born abroad, fallowing the definition adopted by Statistics Norway (SSB) and used in a previous study [14].

The regression model is described by the equation

$$\log \mu_t = \theta_0 + \theta_1 x_t \tag{6}$$

where x_t is the count of the infections at time t for a specific age-group and ethnic background.

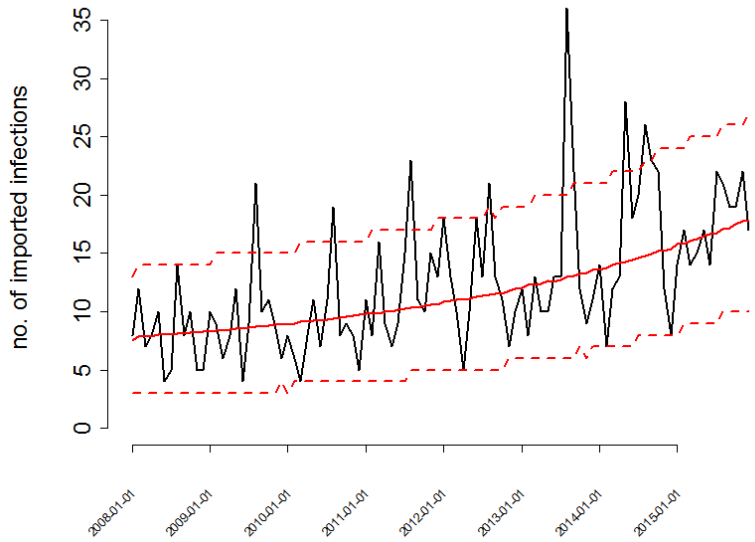


Figure S2: Number of infections acquired abroad. The black line is the monthly number of infections notified in the national registry as acquired abroad. The red line represents the number of infections acquired abroad reproduced by the model and averaged over 5000 simulations, the red-dashed lines are the 95% confiedence intervals.

Table S1: Parameter estimates for the number of infections acquired abroad.

age-group	ethnic-background	model	parameter	estimate	standard deviation
0-19	Norwegian	$\log \mu_t = \theta_0$	θ_0	0.051	0.099
	Immigrant	$\log \mu_t = \theta_0 + \theta_1 x_t$	θ_0	-0.558	0.199
			θ_1	0.022	0.003
20-39	Norwegian	$\log \mu_t = \theta_0$	θ_0	0.77	0.07
	Immigrant	$\log \mu_t = \theta_0 + \theta_1 x_t$	θ_0	0.005	0.161
			θ_1	0.017	0.002
40-69	Norwegian	$\log \mu_t = \theta_0$	θ_0	0.85	0.07
	Immigrant	$\log \mu_t = \theta_0 + \theta_1 x_t$	θ_0	-0.61	0.23
			θ_1	0.015	0.003
70+	Norwegian	$\log \mu_t = \theta_0$	θ_0	-0.57	0.14
	Immigrant	$\log \mu_t = \theta_0$	θ_0	-2.16	0.30

1.3 Infection-control in healthcare institutions

For healthcare settings, we implemented in the model the following infection-control measures based on the search-and-destroy policy described in the Norwegian national MRSA guidelines [11].

Screening at entrance in hospitals

Persons admitted to the hospital are tested if they present symptoms (infected individuals) or they have been abroad in the past 12 months[1], or in case of positive persons detected in their family within the previous year.

Isolation

In hospitals, persons found positive to MRSA are isolated. As a precautionary measure,individuals who are infected at the time of hospitalization are directly placed in isolation. We assumed that patients remain isolated for the whole remaining part of their hospitalization period.

Work restriction

Work restriction measures are applied to healthcare workers found positive to MRSA. During their sick-leave, ranging between 5 and 10 days, healthcare workers are successfully decolonized.

Households screening

For healthcare workers found positive to MRSA, all family members are tested and, in case of positive results, decolonized.

Screening in healthcare institutions

MRSA positive cases discovered among healthcare workers or non-isolated patients in hospital trigger a screening of all patients and healthcare workers linked to the ward.

In nursing homes, after 2010 we implemented in the model the screening of the patients and healthcare workers in the institutions in case of an unexpected MRSA finding. The intensification of the infection control measures has been introduced in Norway in response to large outbreaks occurred before 2010 in these settings [15].

Decolonization therapy

Decolonization therapies are offered to all discovered cases of MRSA colonizations and infections in hospitals and nursing-homes, as well as to all individuals in the community developing an infection. We assumed that infected individuals return susceptible after treatment. For MRSA carriers we set the efficacy of decolonization to 90% [16] .

1.4 Model calibration

Preliminary calibration analyses pointed to a negligible role of workplaces, schools and random contacts in the transmission of MRSA. Therefore, the values assigned to the transmission rates β_w and β_r were fixed to zero. Eventually, we considered seven free parameters and fixed all others from literature (Table S2). The free parameters are: 1-3) the transmission rates for households, hospitals and nursing homes; 4) the progression rate from colonization to infection in the general population; 5-7) the initial prevalence in the community, hospital healthcare workers, and nursing home patients.

Given the running time of a single model simulation (about 10 minutes on a 2.6 GHz core) and the need to deal with model stochasticity, sequential calibration approaches such as Monte Carlo Markov Chain are unfeasible. Therefore, we adopted a calibration procedure where computation of the model outputs under different parameter sets could be parallelized, as standard in these

[1] we assumed that 70% of the patients who traveled abroad are screened at hospitalization, based on national registry data

Table S2: Parameters' values and source.

parameter (unit)	value	source
proportion of person with foreign background in the population	16%	[17]
nurses to bed ratio in hospital	0.2	[9]
nurses to bed ratio in nursing home	0.3	[10]
length of stay in hospital for long-term patients in nursing homes (day)	4.3	[18]
colonizations to infections ratio for imported cases	10:1	[19]
duration of carriage (day)	365	[20, 21]
initial prevalence among hospital patients	1%	[22]
initial prevalence among nurses in nursing home	1.5%	[23]
screening probability for hospitalized patients with travel history	0.7	national registry data
sensitivity of MRSA test	0.825	[24]
turn around time for MRSA test (day)	3	[24]
probability of successful decolonization for MRSA carriers	0.9	[16]
progression rate from colonization to infection in hospital (day^{-1})	$1.6 \cdot 10^{-3}$	[12]
progression rate from colonization to infection in ICU (day^{-1})	$6 \cdot 10^{-3}$	[12]
progression rate from colonization to infection in nursing homes (day^{-1})	$1.2 \cdot 10^{-4}$	[13]
transmission rate in households, β_h (day^{-1})	$4.4 \cdot 10^{-3}$	calibration
transmission rate in hospitals, β_{hosp} (day^{-1})	$5.7 \cdot 10^{-2}$	calibration
transmission rate in nursing-homes, β_{nh} (day^{-1})	$3.2 \cdot 10^{-3}$	calibration
progression rate from colonization to infection in the community, δ_C (day^{-1})	$3.9 \cdot 10^{-5}$	calibration
initial prevalence in community, P_0^C	0.16%	calibration
initial prevalence in nursing-homes, P_0^{nh}	1.8%	calibration
initial prevalence in hospitals among nurses, $P_{0\,HCW}^{\;\;hosp}$	1.9%	calibration

cases (e.g. [25, 26]), so that simulations could be run on a High Performance Computing facility. We used Latin Hypercube Sampling to efficiently explore the parameter space by obtaining the same resolution of a random sampling procedure with fewer samplings [27]. For each sampled set of parameters, P_i, we ran a simulation over a period of 8 years and we computed the likelihood of the yearly time series of infections acquired in Norway in community, hospitals and nursing-homes, and of the prevalence in household contacts of MRSA carriers [28]. The likelihood function is defined by the product of three Poisson likelihoods and a binomial likelihood,

$$L(P_i) = L_{hh} \cdot L_{hosp} \cdot L_{nh} \cdot L_{hhprev} \tag{7}$$

The first three terms in equation 7 represent the Poisson likelihood of the number of infections in households, hospitals and nursing homes respectively. They are defined as

$$L_x = \left(\prod_{y=1}^{Y} \frac{e^{n_{x,y}} n_{x,y}^{o_{x,y}}}{o_{x,y}!} \right) \tag{8}$$

where $n_{x,y}$ and $o_{x,y}$ are respectively the number of infections produced by the model and observed in the data in setting x (i.e., households, hospitals, or nursing homes) during the y-th year of the simulation. Y is the final and 8-th year of the simulation, corresponding to 2015.
The fourth term of equation 7, L_{hhprev}, represents the binomial likelihood,

$$L_{hhprev} = \binom{N}{K} p^K (1-p)^{N-K} \tag{9}$$

where $K = 42$ is the number of positive cases out of a total of $N = 114$ familial contacts screened in [28], and p is the average prevalence of MRSA in household members of carriers, as simulated by the model.

The calibration procedure occurred in three steps:

1. We ran 10 000 LHS samplings from very broad parameter ranges, reported in Table S3. We used the likelihood score to select a hypercubic sub-region of the parameter space with plausible parameter values for further exploration. In particular, we selected the maximum

and minimum parameter values from the first percentile of the overall likelihood distribution as boundaries of the selected hypercube.

2. We performed a finer exploration of the hypercube selected at the end of step 1 by LHS sampling 100 000 new parameter sets, and we selected parameter sets in the top 0.5 percentile of the new likelihood distribution (Fig. S3).

3. To control for stochastic fluctuations in likelihood values associated to each parameter set, we ran 50 simulations for each of the 500 parameter sets identified in step 2, and we computed the likelihood after averaging model outputs over all stochastic repetitions. Fig. S4 shows that this number of simulations is sufficient for the likelihood to converge to stable values for all parameter sets. The 100 parameter sets with optimal likelihood values were finally selected.

The distributions of selected parameter values are shown in Fig. S5. All selected distributions display a limited variability and their range is well inside the initial range of exploration. The means and 95% credible intervals computed from these distributions are reported in Table S3.

The outputs of the 5 000 simulations, obtained from 50 repetitions of the 100 best parameter sets, were pooled together and analyzed to produce the results reported in the main text. Fig. S6 shows that the variability in parameter values has a limited effect on the model-estimated incidence of infections, and that stochastic variability has a similar impact than random fluctuations observed in data.

Table S3: Parameter estimates obtained at the end of the calibration procedure and corresponding initial range of exploration.

parameter (unit)	mean	95% CI	initial range
β_h (day^{-1})	$4.4 \cdot 10^{-3}$	$2.6 \cdot 10^{-3}$, $6.4 \cdot 10^{-3}$	10^{-3}, 10^{-1}
β_{hosp} (day^{-1})	$5.7 \cdot 10^{-2}$	$4.9 \cdot 10^{-2}$, $6.4 \cdot 10^{-2}$	$5 \cdot 10^{-3}$, 10^{-1}
β_{nh} (day^{-1})	$3.2 \cdot 10^{-3}$	$2.7 \cdot 10^{-3}$, $3.8 \cdot 10^{-3}$	10^{-4}, $\cdot 10^{-2}$
δ_C (day^{-1})	$3.9 \cdot 10^{-5}$	$2.8 \cdot 10^{-5}$, $5.1 \cdot 10^{-5}$	10^{-6}, 10^{-4}
P_0^C (%)	0.16	0.10, 0.19	0.01, 0.5
P_0^{nh} (%)	1.8	0.9, 2.6	0.5, 5
P_{0HW}^{hosp} (%)	1.9	1.2, 2.4	0.5, 5

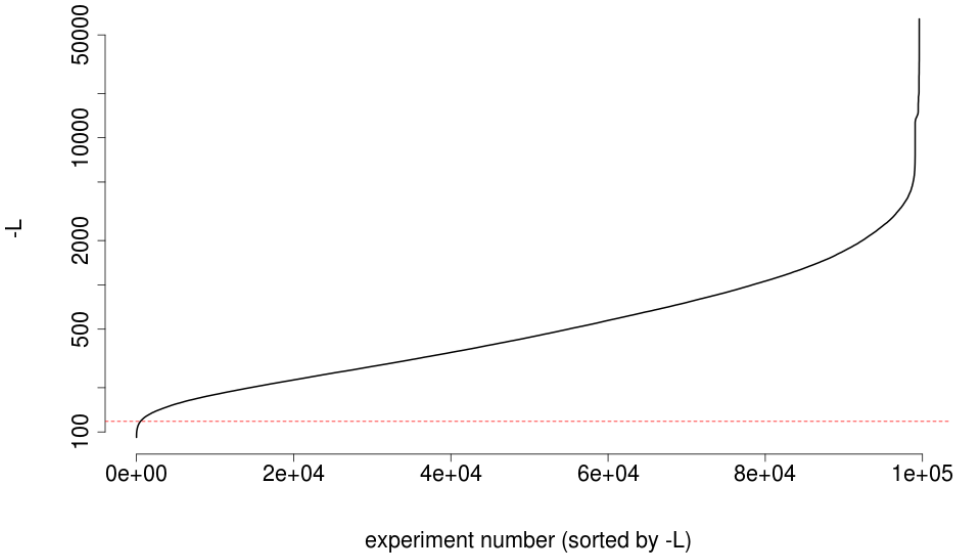


Figure S3: Distribution of the log-likelihood for the 100 000 LHS samples in step 2, sorted by increasing value of the likelihood. The red, dashed line represents the 0.5 percentile of the distribution. Note that the y-axis is log-scaled.

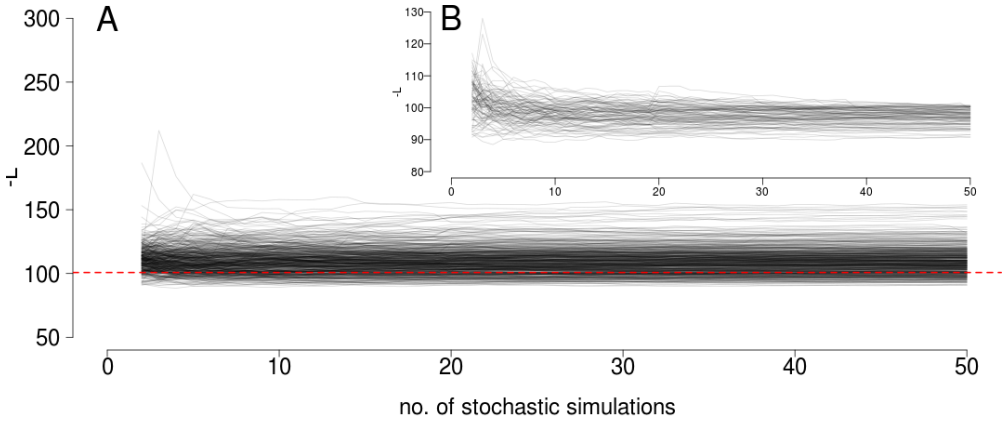


Figure S4: A) Log-likelihood of the outputs from the best 500 parameter sets in step 3, averaged over the first x stochastic repetitions. The red dashed line represents the 100th best value of the log-likelihood averaged over 50 iterations. B) Log-likelihood of the outputs from the 100 selected parameters sets, averaged over the first x stochastic repetitions.

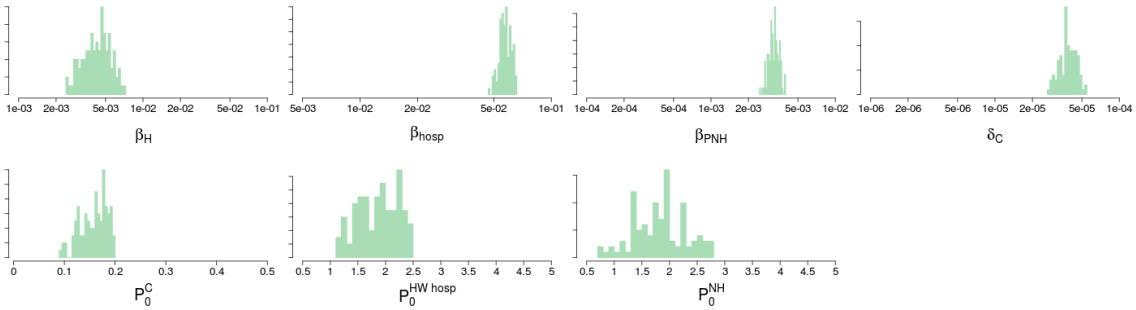


Figure S5: Distribution of the seven free parameters (β_h, β_{hosp}, β_{nh}, δ_C, P_0^C, P_0^{nh} and P_0^{HWhosp}) at the end of the calibration phase. Four parameters, β_h, β_{hosp}, β_{nh} and δ_C, are represented on a log-scale

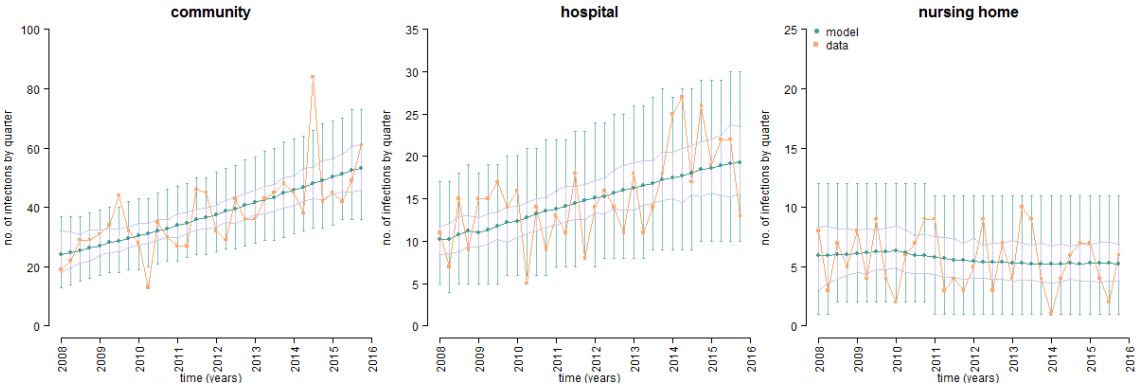


Figure S6: Quarterly time series of the number of infections reported in community, hospitals and nursing homes between 2008 and 2015. The orange line represents infections reported in the Norwegian national registry; the green line is the average of the model outputs over the 5 000 simulations. The violet shaded areas show the 95% confidence intervals of the average number of infections over the 50 stochastic runs, computed for each parameter set, and thus represent the parameter-related uncertainty. The green bars show the 95% confidence intervals computed over the full distribution of 5 000 model outputs.

Table S4: Distribution of infections by setting of acquisition. Mean proportions of infections by setting of acquisition for each setting where infection was developed. 95% confidence intervals are reported within brackets.

		setting of acquisition			
		imported	hospital	community	nursing home
setting of infection	community	11.5 (7.6-15.9)	34.0 (21.6-48.1)	54.5 (37.8-69.8)	0.0 (0.0-1.0)
	hospital	1.8 (0.5-3.5)	83.2 (74.2-90.1)	11.6 (5.4-20.0)	3.4 (1.4-5.9)
	hospital ICU	2.7 (0.0-7.0)	74.8 (60.7 - 86.8)	17.4 (6.4-31.0)	5.1 (0.0-11.4)
	nursing home	0.0 (0.0-0.0)	16.3 (8.8-25.9)	0.4 (0.0-1.8)	83.3 (73.4-90.8)

2 Additional results

2.1 Distribution of infections by setting of acquisition

Table S4 reports the proportion of infections by setting acquisition, corresponding to numbers reported in Fig. 5 in the main text.

2.2 Incidence of infection in healthcare workers

Fig. S7 shows a strong agreement between the observed and model-predicted number of infections reported in healthcare-workers over the whole study-period, assuming a risk of infection among colonized healthcare workers equal to that of the general population. This result, which was not imposed by our calibration procedure, validates the model estimate for the prevalence of colonization among healthcare workers.

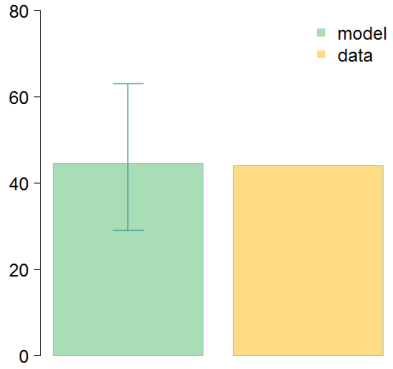


Figure S7: Number of infections among healthcare workers from 2008 and 2015. The light green bar is the average number of infections reproduced by the model with the 95% confidence intervals. The yellow bar is the number of infections reported in the Norwegian national registry data.

2.3 Forecasting

The results of the model presented in the main manuscript cover a period of time of eight years. In additional analyses we performed a 5 years forecast, assuming that the number of imported cases continue to follow the exponential increase described by the Poisson regression models fitted to the data in the period 2008-2015 (Fig S8). The predictions showed a clear rise in the community; at the end of the forecast, the prevalence in the general population reached a level of 0.49% (95%CI

0.16-0.91%), corresponding to a 32% increase compared to its value 5 years earlier. In the same temporal interval, the prevalence among hospital patients increased by about 10% at the end of the forecast with a final value of 1.25% (95%CI 0.52-1.99%). A slight rise is visible in the mean number of infections in nursing homes, although the level did not change significantly. The prevalence at the end of the 5 years was estimated to be 1.91% (95%CI 1.28-2.70%).

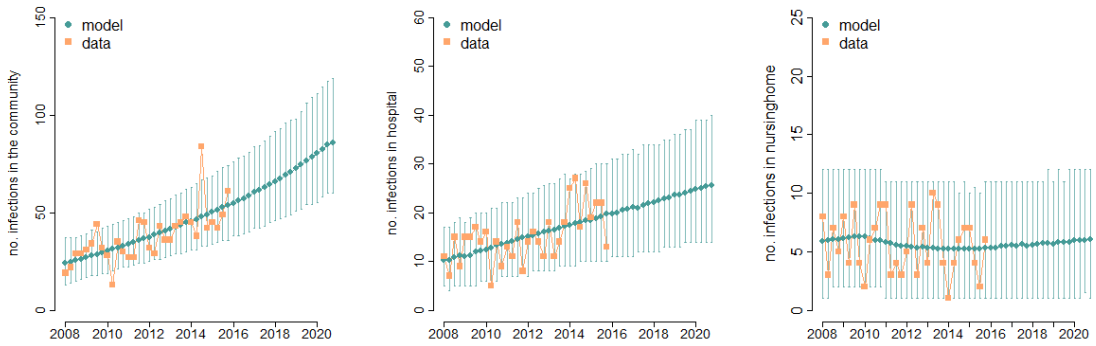


Figure S8: Number of infections predicted by the model over a five years horizon. The orange line represents infections reported in the Norwegian national registry from 2008 to 2015; the green line is the five-year model prediction averaged over the 5 000 simulations. The green bars show the 95% confidence intervals computed over the full distribution of 5 000 model outputs.

2.4 Sensitivity analysis

2.4.1 Ratio of imported colonizations to infections

The number of imported asymptomatic MRSA carriers is difficult to measure in real life; therefore we estimated the number of imported colonizations on the basis of imported infections, and considering a 10:1 ratio for asymptomatic:symptomatic carriers [19]. To test the impact of this assumption we performed two sets of 5000 simulations changing the ratio to 5:1 (scenario A) and to 20:1 (scenario B). We did not find significant differences in the epidemiological characteristics and transmission dynamics of MRSA, compared to conclusions derived from the main analysis.

The community remained the primary route of transmission of MRSA, with 48.9% and 50.4% of the colonizations acquired in this setting in scenarios A and B respectively. Hospitals followed with 37.9% and 27.7% of transmissions. Both scenarios resulted in a prevalence of carriage in the community in 2015 which was very close to the 0.37% estimated in the main analysis (0.3% in scenario A, 0.5% in scenario B).

The age-specific prevalence of carriage was higher in scenario B especially among younger age-classes (Fig. S9), which generally travel more frequently and are more exposed to MRSA acquisition in foreign countries. The lower increase of the prevalence among the older age-groups is also a consequence of the households' structure, since elderly persons usually live in households of small size (Fig. S10) and thus they also have a low risk of acquiring MRSA by contact with other family members infected abroad. However, prevalence estimates in the two scenarios were within the 95% confidence intervals in all cases.

For what concerns infections, in both scenarios an important share was still acquired in hospital setting (48.1% in scenario A and 37.9% in scenario B; Fig S12). The increasing number of colonizations imported from abroad mainly impacted the number of infections developed in the community setting (Fig S13), where the proportion of infections deriving from the import of MRSA changed from 6.5% (scenario A) to 13.4% (scenario B). The source of acquisition for infections developed in hospitals and nursing homes are substantially unchanged in the two scenarios (Fig. S14 and S15).

The importation of MRSA from abroad has mainly an impact on the community, particularly on the prevalence of young and adult individuals, who are less frequently hospitalized compared to elderly people. Thus, the effect of the uncertainty of the number of imported colonizations on the model's calibration would be primarily confined on the infection rate in households, δ_C, (given that the transmission rate, β_h, is constrained by the data on prevalence within household contacts of colonized individuals). Considering the community prevalence in scenario A (0.3%; where we

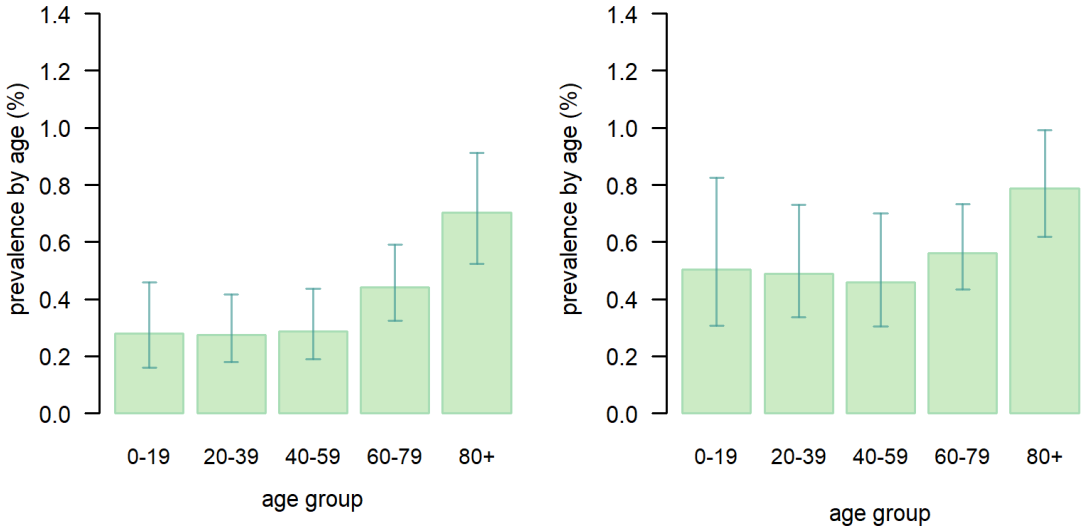


Figure S9: Prevalence by age-groups for scenario A (a) and scenario B (b).

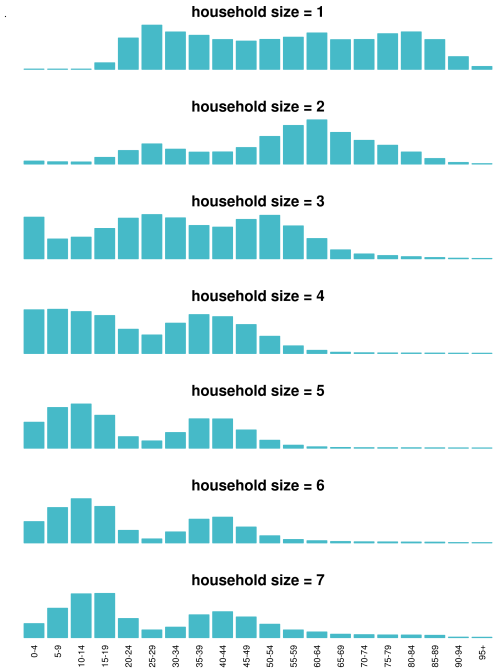
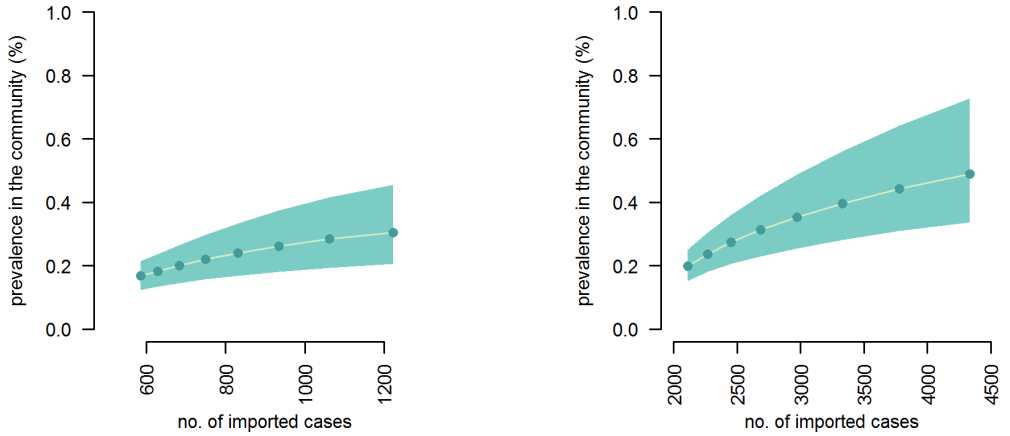


Figure S10: Age structure of households by size reproduced by the individual-based model.

halve the colonization-to-infection ratio in imported cases), to obtain the number of infections reported in the national registry, we would need an infection rate of approximately 4/3 (i.e. 33% higher) than the one estimated in the baseline. Conversely, considering the prevalence in Scenario B (0.5%), the same number of infections would be obtained with a 20% reduction in the estimated infection rate.

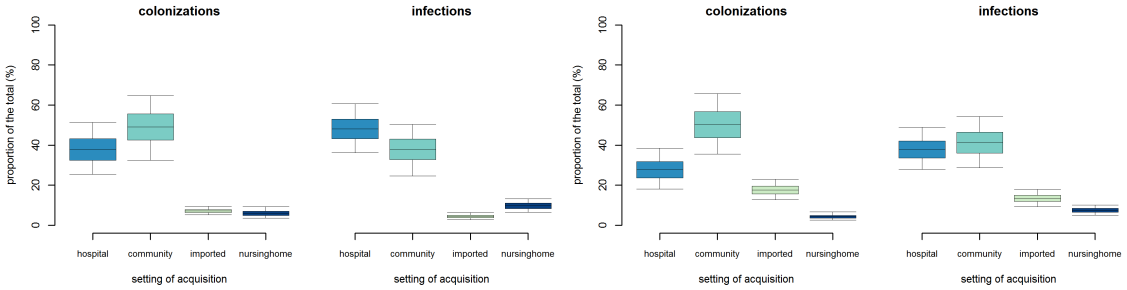
2.4.2 Import of MRSA from abroad

To evaluate the effect of importation levels on MRSA spread, we performed model simulations considering a fixed importation over the whole study period. We considered importation rates having values equal to 1, 2, 5, 10, 20 and 30 times the rate observed in 2008 (i.e., approximately 1000 cases per year). Fig. S16 shows the prevalence of MRSA at the end of the study period in



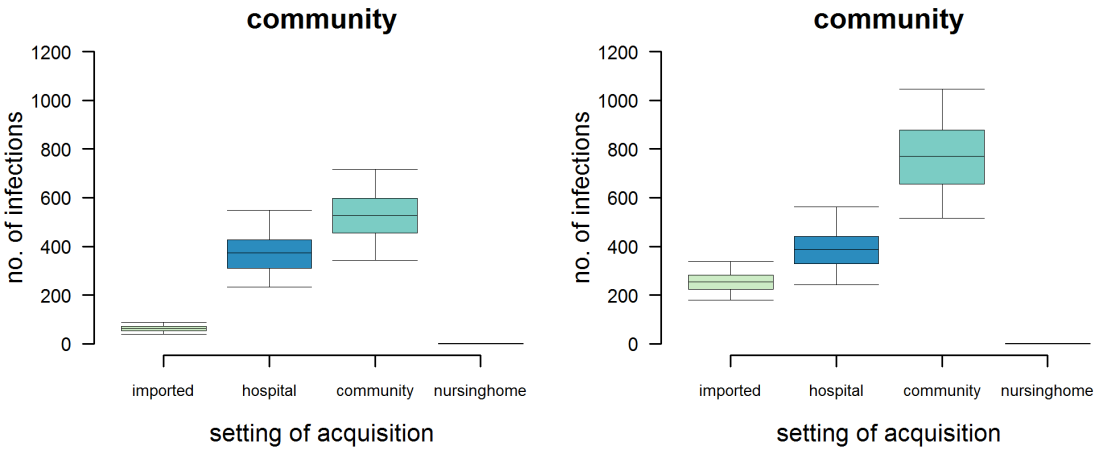
(a) (b)

Figure S11: Scatter plot of the prevalence in the community as a function of the number of imported cases for scenario A (a) and scenario B (b).



(a) (b)

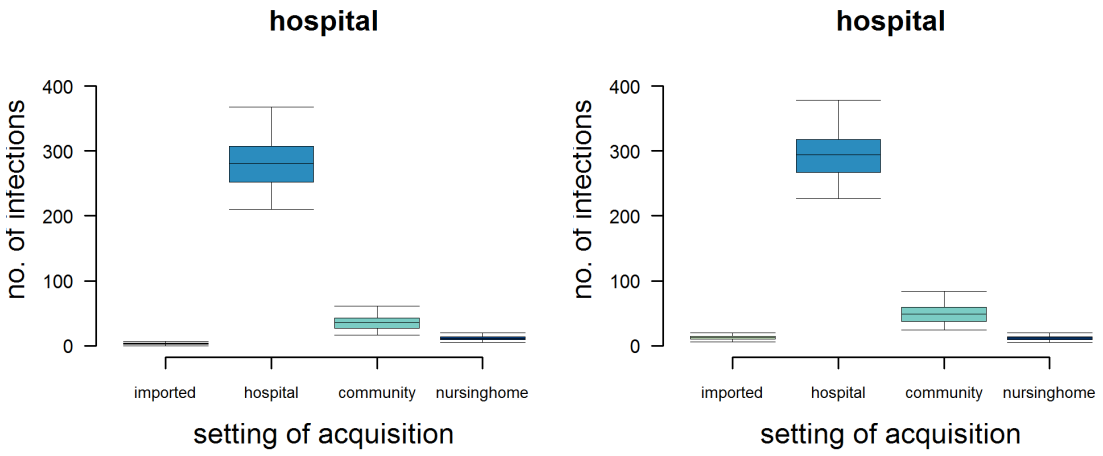
Figure S12: Proportion of infections and colonizations by setting of acquisition for scenario A (a) and scenario B (b).



(a) (b)

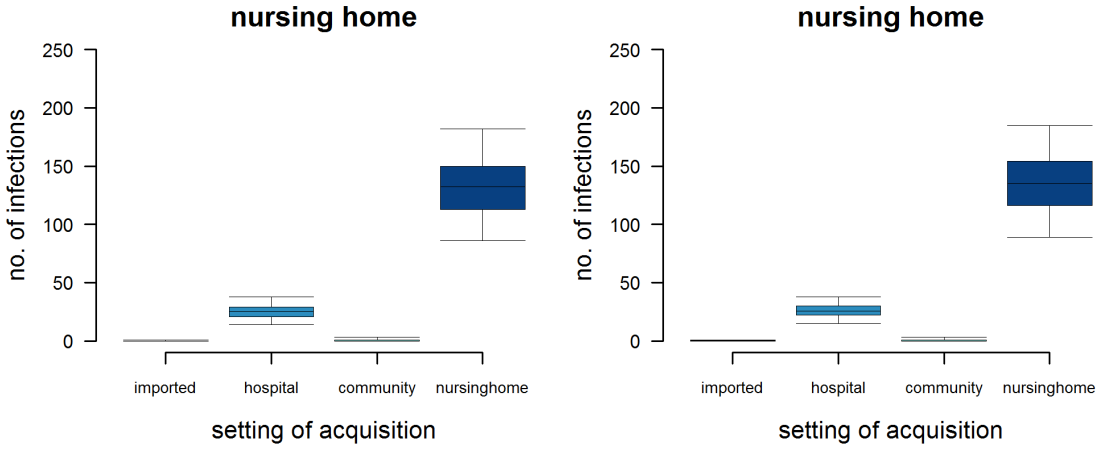
Figure S13: Number of MRSA infections in the community by setting of acquisition for scenario A (a) and scenario B (b)

different settings for different scaling factors. In the case of fixed importation rates, we observed a linear increase in prevalence rates for all settings. The direct import of MRSA in the general population mainly impacts the community, as highlighted by the steeper growth of the prevalence. This increasing circulation among the general population generates also a pressure on the hospital



(a) (b)

Figure S14: Number of MRSA infections in hospital by setting of acquisition for scenario A (a) and scenario B (b)



(a) (b)

Figure S15: Number of MRSA infections in nursing home by setting of acquisition for scenario A (a) and scenario B (b)

institutions resulting in a significant growth of the prevalence in these settings. The increase of importation has a minor impact on the nursing homes, due to the lower interactions with the community; the growth in this setting is almost entirely attributable to the rise in the prevalence of carriage in hospital setting, affecting patients transferred between hospital and nursing homes.

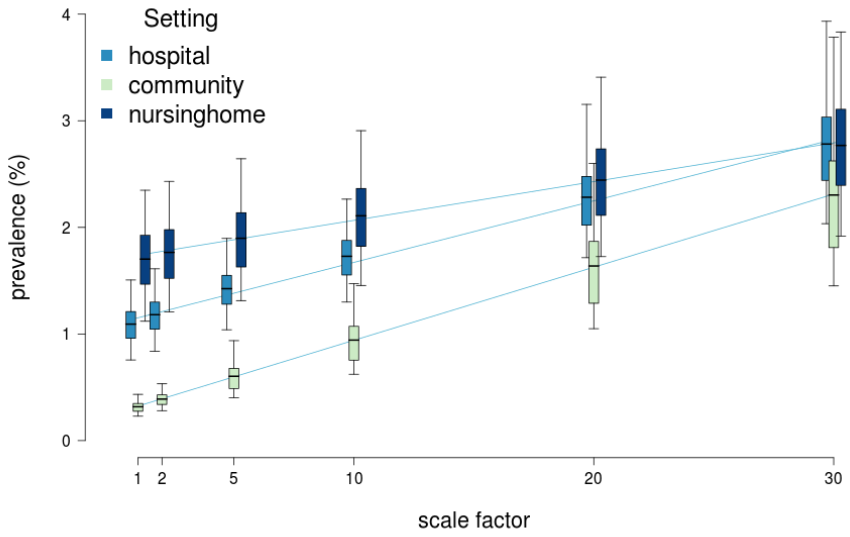


Figure S16: Prevalence by setting as a function of different levels of imported MRSA cases. The x-axis reports the multiplication factors by which the level of import cases reported in 2008 in Norway (approximately 1000 colonizations an infections) was increased. Linear regression models were fitted to the data points. The angular coefficients (θ) for the three curves are: θ_{hosp}=0.057 (95 %CI 0.049-0.065); θ_{comm}=0.068 (95 %CI 0.067-0.069); θ_{nh}=0.036 (95 %CI 0.031-0.041).

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