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Quantitative Assessment of Human MRSA Risks from Swine

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The public health community, news media, and members of the general public have expressed significant concern that methicillin-resistant *Staphylococcus aureus* (MRSA) transmitted from pigs to humans may harm human health. Studies of the prevalence and dynamics of swine-associated (ST398) MRSA have sampled MRSA at discrete points in the presumed causative chain leading from swine to human patients, including sampling bacteria from live pigs, retail meats, farm workers, and hospital patients. Nonzero prevalence is generally interpreted as indicating a potential human health hazard from MRSA infections, but quantitative assessments of resulting risks are not usually provided. This article integrates available data from several sources to construct a conservative (plausible upper bound) probability estimate for the actual human health harm (MRSA infections and fatalities) arising from ST398-MRSA from pigs. The model provides plausible upper bounds of approximately one excess human infection per year among all U.S. pig farm workers, and one human infection per 31 years among the remaining total population of the United States. These results assume the possibility of transmission events not yet observed, so additional data collection may reduce these estimates further.

KEY WORDS: Bayesian risk analysis; methicillin-resistant *Staphylococcus aureus*; microbial risk assessment; MRSA

1. INTRODUCTION: HOW LARGE IS THE HUMAN HEALTH RISK FROM MRSA IN SWINE AND PORK?

Recent news stories, and many websites and blogs, have warned that antibiotic-resistant bacteria from pig farms may threaten public and worker health. One widely discussed concern is that animal antibiotics used on farms create selection pressures that favor the spread of antibiotic-resistant "superbugs," such as methicillin-resistant *Staphylococcus aureus* (MRSA).[1] However, these stories have lacked a quantitative discussion of *how many* excess deaths, treatment failures, or days of illness each year are caused in the United States by MRSA arising from pig (or other livestock) production. Most human cases of MRSA are health-care associated, and usually arise from inadequate hand washing and infection control in hospitals.[2] How many cases of MRSA infections and fatalities per year arise among hospital patients, butchers, slaughterhouse workers, farmers, or the general public from livestock operations, meat handling, and consumption therefore remains to be addressed. Responsible risk management is supported best by understanding how large the human health risks are now, and how much they would be changed by proposed interventions.

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2. POTENTIAL HUMAN MRSA HAZARDS RELATED TO PIGS AND PORK

This section takes inventory of what is known about adverse human health outcomes that might be caused by exposure to ST398 MRSA from swine

and pork. Although ST398 MRSA has been detected in other food animals, it has mostly been associated with pigs. On a worldwide basis, ST398 has been detected in veal calves, cattle, poultry, and sheep; however, such instances are much less common than in swine, and have not been reported in the United States.[3] Similarly, while a number of studies have detected *S. aureus*, and less frequently, MRSA strains, in a variety of retail meats in the United States, ST398 seems to be found exclusively in pork.[4–6] The purpose of the following subsections, then, is to identify sources of swine- and pork-related risk (i.e., hazards) that pose nonnegligible human health risks, so that these can be quantified further.

2.1. Consumer Exposure to MRSA via Pork Meat Poses Little Risk

Consumption of pork meat raises the logical possibility of three types of exposure and harm from MRSA: invasive infections by MRSA acquired from meat; noninfectious food poisoning by MRSA enterotoxins (as with other strains of *S. aureus*); and colonization (with the possibility of subsequent opportunistic infection) by MRSA from pork products. Each of these is briefly considered next. We find that only the last, colonization, appears to pose a potentially significant risk in the United States.

- *Invasive infection by MRSA consumed in pork products.* No case of a livestock-associated (ST398) MRSA *infection* transmitted via the food supply (or otherwise) has ever been found in the United States.[7,8] Worldwide, only one case of invasive infection by ST398 MRSA after ingestion of contaminated food has ever been identified, in a highly immunocompromised individual in a Dutch hospital.[9] Given the large quantities of pork consumed for decades without other cases being identified, the threat to the U.S. population for this pathway appears to be near zero.
- *Enterotoxicosis by ST398 MRSA.* Although staphylococcal enterotoxicosis is a common form of food poisoning caused by *S. aureus* toxins in food, the pig-associated (ST398) strains of MRSA do not produce these toxins, as they lack the enterotoxin genes needed to express them.[10] No association between consumption of pig meat and increased risk of such food poisoning has been found.[11] Thus, the threat of food poisoning by ST398 MRSA in pork products also appears to be insignificant or nonexistent.
- *Colonization with ST398 MRSA encountered via the food-handling process.* Although the probability of this type of colonization appears to be very low for the average consumer, as discussed next, it is somewhat higher for people in meat-handling professions such as butchers and slaughterhouse workers.[12,13] This assessment therefore includes quantification of the risks of colonization arising from food handling.

2.2. Direct Exposure to Pigs Can Increase Risk of Colonization with MRSA

Several studies have found elevated risk of MRSA colonization in people working closely with pigs and other livestock,[14] including farm workers,[15] veterinarians,[16] and slaughterhouse workers.[12] However, subsequent infections have not been documented in the United States,[8,17] although there have been some reports of minor soft tissue infections in other countries.[18,19] Because MRSA colonization has been observed among pig farm workers on MRSA-positive farms, even in the United States,[15] the possibility of subsequent infections cannot be ruled out. These risks, too, are therefore quantified in the following sections.

2.3. Hospital Outbreaks of ST398 MRSA Are Extremely Rare

The only known death associated with ST398 MRSA occurred in a medically compromised person in a Spanish hospital who sometimes worked on a pig farm.[20] There have also been limited reports of person-to-person transmission of ST398 MRSA in Dutch hospitals;[21,22] however, there has been only one reported instance of an outbreak of ST398 MRSA among patients,[23] and the study report did not clearly differentiate between colonization and infection. Because person-to-person transmission has been suggested, the possibility of future outbreaks remains, and is quantified in the following sections.

2.4. Community Outbreaks of ST398 Have Not Been Observed

No community outbreaks of ST398 MRSA have been documented, so community outbreaks are probably even less likely than hospital outbreaks.

This may be due to the relatively transient nature of most ST398 colonizations. Although some authors have recently argued that living near pigs raises the risks of colonization,[14] the statistical methodology behind such ecological associations is suspect, and such reported associations are often meaningless—random spatial trends alone can create statistically significant regression coefficients; and spatial location can be a confounder for spatially distributed exposure and response variables.[24] Due to its extremely low likelihood, we have not attempted to compute a risk for community outbreaks of ST398 MRSA.

3. FOOD-HANDLING HAZARDS

3.1. ST398 MRSA is Found in Retail Pork

MRSA, including ST398, is occasionally found in retail meats, including pork. Recent studies conducted in various parts of the United States tested retail pork products for the presence of ST398 MRSA. Meat samples are typically agitated in a rinsate solution whose contents are then cultured and analyzed. Table I summarizes relevant data from these studies.

3.2. MRSA Colonization from Food Handling is Possible

A study in the Netherlands of workers who came in frequent contact with raw meat (institutional kitchens and cold meat processing) found no MRSA colonization in 95 participants[28] although MRSA was present on 2 of 10 (20%) pork samples from the same locations and 3 of 26 samples of veal and chicken. A recent study of butchers in Hong Kong did find cases of MRSA colonization.[29] Seventeen of 300 butchers (5.7%) carried MRSA, and 10 of these carried strains commonly found in local swine (3.3% of total). A separate study of pig carcasses at markets in Hong Kong found that 16 of 100 carcasses tested positive for swine-associated strains of MRSA.[30] However, MRSA carriage in the Hong Kong general population is rare (~1.4%) and is largely associated with working in healthcare.[31] Therefore, it is plausible that meat handling can be a risk factor for MRSA colonization in Hong Kong, and possibly elsewhere.

In summary, our hazard identification suggests that the major nonnegligible risks from pig-associated MRSA arise from colonization, with potential for subsequent infection. The following sections seek to quantify these risks.

4. QUANTIFYING PIG-ASSOCIATED MRSA COLONIZATION POTENTIAL

4.1. Quantitative Estimation of Colonization Potential for Professional Food Handlers in the United States from Pork Meat

To quantify uncertainty about the true proportion of ST398 MRSA-colonized food handlers in the United States, we apply Bayesian conjugate prior analysis. We first assume a standard uniform prior distribution for the true but unknown proportion of colonized food handlers, and then adjust this starting assumption by conditioning on the Dutch data above (showing 0 colonizations among 95 workers). The uniform prior distribution is a deliberately conservative assumption, in that it implies that in the absence of data, half of all food handlers are expected to be colonized, which is an order of magnitude greater than the empirically observed fractions just reviewed. Thus, we begin with a deliberately exaggerated (risk overestimating) assumption, and then use data to revise it downward via Bayes's Rule. As the most recent and relevant available data source, we use the Netherlands study[28] showing $s = 0$ positive observations among $n = 95$ workers. Bayesian conditioning of the uniform prior on these data yields a posterior distribution (a Beta(s+1, n – s +1) = Beta(1,96) posterior distribution) with a mean of (s+1)/(n+2) = 0.0103.

To determine a fraction attributable to pork handling alone, we note that pork comprises approximately 55% of total meats consumed in the EU.[32] MRSA prevalence on pork in the Netherlands is actually slightly *lower* than the average for all retail meats. A large-scale Dutch study found MRSA on 264 of 2,217 (11.9%) total retail meat samples, 10.7% of retail pork samples, but even higher rates on several other retail meats: turkey (35.3%), chicken (16.0%), veal (15.2%) and also beef (10.6%), lamb and mutton (6.2%), fowl (3.4%), and game (2.2%).[33] Based on these figures, it is reasonable to assume that somewhat less than 55%, perhaps roughly 50%, of MRSA prevalence among Netherlands food handlers could be due to pork. To account for a high degree of uncertainty, we will further assume that the true fraction can be described by a uniform probability distribution with 0.50 as a mean,

Table I. ST398 MRSA Prevalence Data from Retail Pork in the United States

Reference	Samples	Portion Size	Rinse	ST398 MRSA Positive	Rate
Ref. 5	300	25 grams	225 mL	1	0.0033
Ref. 4	26	Unknown	250 mL	1	0.0385
Ref. 25	143	Whole chop, 1 in cube	Unknown	7	0.0490
Ref. 26	135	25 grams	225 mL	5	0.0370
Ref. 27	395	100 grams minimum	250 mL	26	0.0658
Overall	999			40	**0.0400**

and [0.30, 0.70] as a plausible range. These endpoints are somewhat arbitrary, but suffice to indicate that the true fraction might differ from the point estimate of 50%.

For the United States, Table I summarizes data from recent retail pork sampling studies. ST398 MRSA prevalence in retail pork in the United States is about 37.38% (0.04/0.107) of the MRSA prevalence in the Netherlands. In addition, pork as a fraction of total meat processed in the United States is about half (49.11%) (0.2720/0.5538) of that in the European Union.[32] A base case estimate of ST398 MRSA prevalence from pork among U.S. meat handlers is thus about (0.0103 posterior mean for the fraction of food handlers colonized in Netherlands) × (0.50 fraction from pork) × (0.3738 ratio of prevalence in U.S. pork compared to prevalence in Netherlands pork) × (0.4911 pork-processing/consumption ratio) ≈ 0.0009. Substituting an upper 95% value of 0.0307 for the mean of 0.0103 in the beta distribution of Dutch meat handlers discussed above yields an upper-bound estimate of 0.0307 × 0.50 × 0.3738 × 0.4911 = 0.0028, which we will use below.

According to the U.S. Bureau of Labor Statistics, in 2010, there were approximately 382,000 persons in the United States employed as "Butchers and Other Meat, Poultry, and Fish Processing Workers" (includes slaughterers and meat packers).[34] Based on the estimates above, we would expect that about 382,000 × 0.0009 = 357 would be colonized with MRSA attributable to handling pork.

4.2. Quantitative Estimation of Colonization Potential from Consumer Food Handling

This section applies a series of multiplicative factors to convert the MRSA colonization risk among professional meat handlers to a risk to those consumers who also handle pork, based on relative exposure durations per year. Pork is eaten approximately 98.5 times annually per capita in the United States. Approximately 21% of that pork is from fresh cooked products, with another 31% coming from ham,[35] implying an average of approximately 51.22 servings of fresh pork or ham per person per year. An average household size of 2.58 (per 2011 U.S. census data) gives an average of about 51.22 fresh servings per person-year/2.58 person-years per household-year ≈ 19.85 raw pork preparation events per household per year. If each preparation event requires the food handler to be in contact with pork, pork juices, or related working surfaces for up to 15 minutes (a generous estimate), then the average annual contact time per preparer is approximately 4.96 hours. Comparing this to a professional meat handler, who is likely to be in contact with meat, juices, and related working surfaces for approximately 2,000 hours/year, approximately 0.2720 of which is related to pork (as previously discussed), the average U.S. consumer preparer has approximately 4.96/(2,000 × 0.2720) = 0.0091 as much exposure time to pork as a professional meat handler. Assuming that colonization events (e.g., from a concentration of MRSA on meat) are relatively rare, and independent from exposure to exposure, a Poisson model for colonization is appropriate, and colonization risk increases approximately linearly with exposure time.

The implied plausible upper-bound colonization risk to the average consumer preparer is then (0.0028 MRSA colonizations from pork per worker year for professional meat handlers) × 0.0091 = 2.55 colonizations per 100,000 consumer preparer-years (2.55×10^{-5}). This does not attempt to correct for any differences in MRSA exposure concentrations or immunity between professional and consumer meat handlers, but assumes that either can be colonized if suitable rare conditions (e.g., high concentrations of MRSA) are encountered on the meat being handled. Applied to the approximate current number of U.S. households, approximately 315M/2.58 gives an

Table II. Probability Model for Colonization Risk from Handling Pork

Component	Distribution	Mean
Dutch food handler prevalence	Beta(1,96)	0.0103
Pork attributable fraction in Netherlands	Uniform(0.30, 0.70)	0.50
U.S. to Netherlands pork prevalence ratio	Constant (ratio of survey study averages)	0.3738
U.S. to Netherlands pork processing ratio	Constant (ratio of historical processing fractions)	0.4911
Average U.S. meat handler risk/person-year (plausible upper bound)	Product of above (apply to 382,000 workers)	**9.45 E-4**
Consumer to food handler time of exposure ratio	Constant (U.S. pork preparation rates)	0.0091
Average U.S. consumer risk/person-year of colonization (plausible upper bound)	Meat handler risk*0.0091(apply to 315M/2.58households)	**8.6E-6**

estimate of (315,000,000/2.58)*(2.55 × 10^{-5}) = 3,111 additional annual colonizations (but not infections) of ST398 MRSA due to consumers handling pork. To place this in context, the best estimate of total MRSA colonizations in the United States is approximately 2 million.[36]

Table II assembles the above distributions and factors into a probability model whose output is a distribution of probabilities for the average annual per-person risk of being colonized with MRSA from food handling.

The corresponding model equations are:

$$\begin{aligned}&\text{Food Handling Colonizations}\\&\quad = (\text{Dutch food handler prevalence}\\&\qquad \times \text{pork attributable fraction}\\&\qquad \times \text{U.S. prevalence ratio}\\&\qquad \times \text{U.S. processing ratio})\\&\quad \times (\text{U.S food workers}\\&\qquad + \text{Consumer exposure time ratio}\\&\qquad \times \text{U.S.population}).\end{aligned} \tag{1}$$

The mean value for the equation is approximately (9.45E-4)*382,000 + (0.8.6E-6)*122,093,000 = 361 occupational cases of colonization + 1,050 consumer cases of colonization ≈ 1,411 total cases of ST398 MRSA colonization from pork meat per year in the United States.

Table III. ST398 MRSA Colonization Among Pig Farm Workers on ST398-Positive Farms

Location	# Positive	# Farm Workers Tested	Reference
Ontario, Canada	5	9	Ref. 37
Germany	97	113	Ref. 16
Belgium	47	94	Ref. 25
Iowa and Illinois	9	14	Ref. 38
Iowa and Illinois	27	51	Ref. 15
Total	**185**	**281**	

4.3. ST398 MRSA Colonizes Pig Farm Workers

ST398 MRSA in pigs can transiently colonize pig farm workers. Cases of ST398 MRSA transient colonization, with occasional cases of infection (the latter observed only in Europe), occur mostly in individuals having direct contact with livestock, especially pigs. Table III summarizes the available worldwide data on the proportion of colonized pig farm workers on farms where pigs have been colonized.

Pooling these samples for workers on MRSA-positive farms yields an empirical ratio of 185/281. To approximate uncertainty regarding the true proportion, we again use a Bayesian updating of a uniform prior distribution as described earlier. Accordingly, the probability that a pig farm worker in direct contact with pigs is colonized with MRSA is estimated by a Beta($s + 1, n - s + 1$) = Beta(186, 97) posterior distribution, with a mean of (s+1)/(n+2) = 186/283 = 0.66 and a standard deviation of 0.028. This mean and standard deviation make a normal approximation applicable, as the endpoints (0 and 1) are many standard deviations away from the mean.

4.4. Estimating the Number of U.S. Pig Farm Workers

To estimate the number of individuals in the United States in close contact with pigs, it is necessary to consider the number of pig farms by herd size, since the average number of workers per pig is known to decrease with herd size. Otto *et al.*[39] performed an economic analysis of Iowa hog production that estimated direct workers required (for farrow-to-finish operations) as a function of herd size as follows: 150 pigs – 1.4 workers, 300 pigs – 3 workers,

Table IV. Computation of Total Pig Farm Workers in the United States

Herd Size	Workers/ Herd	Percent of Herds	Number of Herds	Total Workers*
1–199	1.4	73.05	55,110	77,155
200–499	3	6.00	4,524	13,572
500–999	6.5	4.76	3,588	23,322
1,000–1,999	10	5.32	4,013	40,130
2,000–4,999	21	7.10	5,356	113,476
5,000+	21	3.78	2,850	59,850
Total		100.0	75,442	**326,505**

*Workers/herd × number of herds.

Table V. MRSA-Positive Farms in the United States and Canada

Location	# Farms MRSA Positive	# Farms Tested	Reference
Ontario, Canada	9	20	Ref. 37
Canada	2	28	Ref. 41
Canada	5	46	Ref. 42
Midwestern United States	12	40	Ref. 43
Iowa/Illinois	4	9	Ref. 15
Minnesota	0	9	Ref. 44
Ohio/N. Carolina	0	6	Ref. 15
Total	**30 (19%)**	**158**	

1,200 pigs – 10 workers, and 3,400 pigs – 21 workers. We obtained the latest available values for the number of herds by size from the National Agricultural Statistical Services.[40] Using approximation and interpolation, we set the labor requirements within the USDA herd size breakouts as shown in column 2 of Table IV. Subsequent calculations shown in the table determine the estimate for total workers on pig farms in the United States.

To model uncertainty, we assume that this estimate of 326,505 for the risk population may be off by as much as 20% (approx. 65,301) in either direction. This subjective uncertainty is expressed as a uniform probability distribution ranging from 261,204 to 391,806. This range is admittedly subjective—other ranges could be considered—but it suffices to explore the sensitivity of results to uncertainty in the size of the heavily exposed worker population.

4.5. Estimating the Proportion of Farms with MRSA

No wide-scale survey of MRSA prevalence on farms has been performed in the United States. However, Table V summarizes recent relevant data points for the United States and Canada. (ABF farms were not included.)

The overall proportion of farms in the United States and Canada positive for ST398 MRSA is $30/158 = 19\%$. To approximate uncertainty regarding the true proportion, we again use Bayesian updating of a uniform prior distribution, yielding a Beta(31, 129) distribution, with a mean of $(s+1)/(n+2) = 31/160 \approx 0.19$, for the distribution of the fraction of MRSA-positive farms.

Table VI. MRSA Colonization Model Parameters

Parameter	Distribution	Mean Value
Number of U.S. pig Farm Workers	Uniform(261,204 to 391,806)	326,505
Fraction of MRSA positive farms	Beta(38, 126)	0.19
P(Colonization| MRSA positive farm)	Normal(0.65, 0.028)	0.66
Estimated U.S. colonizations	Product of above	40,944

4.6. Probability Model for ST398 MRSA Colonization

Table VI assembles the probability distributions derived above into a product-form probability model for the number of annual ST398 MRSA colonizations among U.S. pig farm workers.

The equation for the model is:

$$\begin{aligned}\text{Farm worker colonizations} &= \text{Pig farm workers} \times \text{Fraction MRSA} \\ &\quad - \text{positive farms} \\ &\quad \times P(\text{colonization} \mid \text{MRSA positive}).\end{aligned} \tag{2}$$

5. ESTIMATING THE ANNUAL PROBABILITY OF MRSA INFECTION FOR THOSE COLONIZED

Transient colonization of the human nasal passages (and other mammals) with *S. aureus* is common in the United States, and is usually asymptomatic. Gorwitz *et al.*[45] estimated a prevalence of 28.6% in the United States in 2004. A fraction of these are methicillin-resistant, approximately 1.5% of the U.S. population. Fortunately, only a small fraction of those colonized with MRSA at any moment develop active MRSA infections. Although the relationship between colonization and infection is not fully

understood, in one instance, researchers have shown that more than 80% of bloodstream infections caused by *S. aureus* in hospitalized adults were preceded by colonization of the anterior nares with the same strain.[36] For initial approximation purposes, we assume that the relationship of infected to colonized can be expressed as a fraction, that is, the number of infected/year is a given fraction of those colonized.

An approximate infection rate can be estimated from a MRSA surveillance program conducted in Iowa during and following the initial detection of ST398 MRSA in swine. In a comprehensive study of 1,166 MRSA isolate submissions from this program (invasive cases only) from 1999 to 2006, *no* ST398 strains were found.[46] A total of 343 isolates were from the latest year, 2006. According to a report from the same laboratory,[17] in the years 2007–2009, the following additional numbers of MRSA isolates were submitted to the Iowa University Hygienic Lab by year: 445, 447, and 455. The report states: "To date, MRSA CC398 [i.e., ST398] has not been identified among the invasive MRSA isolates submitted to SHL [State Hygienic Laboratory] from Iowa residents." (Surveillance ended 1/1/2011 and data after 2009 were not provided.) Thus, while ST398 appears likely to be not uncommon among Iowa swine, there are no reported cases of invasive or even soft-tissue infection cases of ST398 in Iowa through the time of the most recent studies. Iowa accounts for 28% of U.S. pork production.[47] This finding is replicated at the national level. The CDC has collected over 12,000 MRSA isolates over recent years that include colonization isolates, infecting isolates, and isolates from animals and from food. The vast majority were collected through the Active Bacterial Core surveillance (ABCs) system.[7] However, no ST398 strains have been detected.[8]

5.1. Probability Model for Infection Given Colonization

If ST398 MRSA was widespread among Iowa hogs by 2006,[48] then for a period of four years, 2006–2009, and likely longer, there were no detected invasive ST398 MRSA cases in Iowa despite the simultaneous significant prevalence among Iowa swine herds and pig farm workers. To put an upper bound on the probable human health risk that is consistent with these observations, we first estimate the mean number of human colonizations of ST398 MRSA in Iowa from 2006–2009 as:

$$\text{Iowa colonization years} = 4 \text{ years} \times 0.28 \text{ of U.S. pigs in Iowa} \times \text{U.S. farm worker colonizations (from Equation (2))} \quad (3)$$

To obtain a distribution of results corresponding to Equation (3), we generated 100,000 random samples from the previously described distributions of uncertain inputs. The mean of the distribution was 55,114. If an estimated 55,114 ST398 MRSA colonization-years in Iowa produced 0 invasive cases, then using a conservative Bayesian analysis similar to that described earlier, we can estimate a plausible upper bound for the annual posterior probability of infection given colonization as belonging to a beta(1; 55,115) distribution with mean 1/55,116 = 1.81E-5.

6. ESTIMATING SECONDARY CASES

While transmission of MRSA among hospital patients is a significant health concern worldwide, the secondary case rate for ST398 MRSA appears to be much lower than that for other types of MRSA. This may be due to the relatively transient nature of ST398 colonizations.[43,49,50]

6.1. Hospital Cases

Wulf *et al.* reported an instance of an apparent outbreak of ST398 MRSA in a Dutch hospital.[23] Bootsma *et al.*[22] identified cases of ST398 transmission from patient to health-care workers (two "outbreaks" involving colonization of one and two workers) in an examination of two large data sets from Dutch hospitals. This and other anecdotal instances reported in Europe indicate that secondary infections are possible.

Van Rijen *et al.*[21] compared the secondary transmission rates for typable MRSA versus nontypable MRSA (presumably ST398) in a Dutch hospital. They reported: "Sixteen patients who carried typable MRSA stayed in the hospital without precautions, for a total of 138 days. Twenty-two of 2139 persons exposed to these 16 patients were shown to be colonized with the index strain. For nontypable MRSA, during 37 exposure days for eight patients, 0 of the 408 exposed patients and health care workers were colonized. Only recently, in 2007, one health care worker was colonized with nontypable MRSA, acquired from a patient who had not been treated in isolation."

6.2. Hospital Estimation Model

Based on these data, a conservative upper bound on the secondary case rate, using Bayesian analysis again, would be that the transmission rate of ST398 MRSA within the hospital is approximately (1/410)/(22/2139) = 0.238 that of non-ST398 strains. A similar result was reported in Wassenberg *et al.*,[51] who computed a relative transmission risk of 0.28. A somewhat lower relative risk was obtain by Bootsma *et al.*[22] of 0.169. The Van Rijen *et al*. data further imply that the average length of stay for ST398 MRSA was (37/8) = 4.625 days versus (138/16) = 8.625 days for non-ST398 MRSA, a reduction ratio of 4.625/8.625 = 0.536. Wassenberg *et al.*[51] obtained values of seven days for ST398 infections and eight days for non-ST398 (0.875 reduction ratio). As discussed in the previous section, the Van Rijen *et al.* results also imply a rate of conversion from colonization to infection in ST398 strains that is approximately (1/4.83) = 0.207 that of non-ST398 strains. Wassenberg *et al.*[51] obtained values of 13 days of exposure before transmission for ST398 cases and three days of exposure for non-ST398 cases, implying a ratio of 3/13 = 0.231 between the two.

We used these data on hospitalization infection dynamics and the mathematical framework of Webb *et al.*,[52] who developed a set of differential equations describing the epidemiological dynamics of MRSA in U.S. hospitals. Their motivation was to determine the conditions under which community-acquired MRSA (CA-MRSA) would displace hospital-acquired MRSA (HA-MRSA) as the dominant infection. They derived a basic reproduction number, R_0, which corresponds to the steady state number of secondary infections per initial infection. Using baseline empirical parameter values, they computed an R_0 for community-associated MRSA (R_O^C) of approximately 0.66 and 0.69 for hospital-associated MRSA R_O^H. To model the hospital dynamics of swine-associated (ST398) MRSA, we modified the Webb *et al.*[52] baseline model for community-associated MRSA based on averages of the parameters discussed above, as summarized in Table VII. To account for uncertainty, we created a stochastic simulation version of the hospital dynamics model. This assumed that input parameters follow log-normal distributions (μ = avg. value, $\sigma = \mu/2$) with the exception of the hand hygiene compliance fraction, which was distributed uniformly between 0.40 and 0.80 versus an original baseline value of 0.60.

Table VII. Adjustment Factors (Right Column) Applied to a Community-Acquired MRSA Hospital Dynamics Model to Obtain Parameters for ST398 MRSA Hospital Dynamics

	Derived from			
Parameter Group	Van Rijen *et al.*[21]	Wassenberg *et al.*[51]	Bootsma *et al.*[22]	Avg.
β_{xy}—transmission rates	0.238	0.28	0.169	0.229
ϕ_{xy}—infection rates	0.207	0.231	NA (colonization only)	0.219
γ_{xy}—discharge rates (1/length of stay)	1/.536	1/0.875	NA (no distinction made)	1/0.706

A total of 100,000 iterations of the simulation model yielded a median reproductive rate for community-associated ST398 MRSA, R_O^C, of approximately 0.0787 (probability > 1 = 0.0016), and a median R_O^H value (hospital associated) of approximately 0.0823 (probability > 1 = 0.0019). These are less than 1/8 of the corresponding values for non-ST398 MRSA when using the same model with the original baseline values. Our QRA model uses a midpoint value of 0.0805 to capture the secondary hospital case rate.

7. QUANTITATIVE RISK ANALYSIS MODEL

Equations (1)–(3), together with a factor for secondary cases, as derived above, can be combined into a probabilistic model for total MRSA infections in the United States attributable to pork. The model can be expressed as

$$\begin{aligned}\text{Expected number of annual infections} &= (\text{Pork-handling colonizations} \\ &\quad + \text{Farm worker colonizations}) \\ &\quad \times P(\text{infection} \mid \text{colonization}) \\ &\quad \times (1 + \text{Secondary case rate})\end{aligned} \tag{4}$$

We implemented the simulation model in the R (version 2.15) statistical programming environment (http://www.r-project.org/) and generated 100,000 random values for each underlying probability distribution to obtain 100,000 random values for food-handling colonizations (Equation (1)), U.S. farm worker colonizations (Equation (2)), and infection

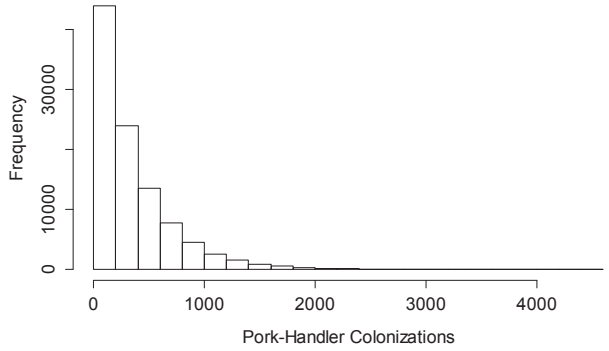

Fig. 1. Distribution of annual MRSA colonizations attributable to pork among professional meat handlers.

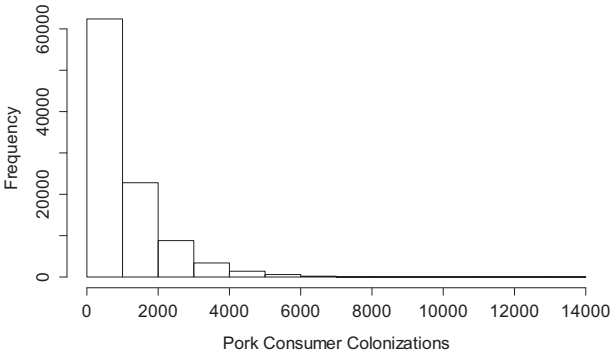

Fig. 2. Distribution of annual MRSA colonizations attributable to pork among pork consumers.

rates (Equation (3)). The secondary case rate of 0.0805 was determined via the separate model just discussed (cf. Table VII). Equation (4), applied to these randomly sampled input values, yielded a distribution of U.S. annual MRSA infections attributable to pigs and pork.

8. RESULTS

The mean number of meat-handler colonizations in the simulation was 358.54 [95% CI—17.29, 1,108.43]. Fig. 1 shows its uncertainty distribution. The mean number of colonizations for pork consumers was 1,042.36 [95% CI: 50.29, 3,182.38], and Fig. 2 shows its uncertainty distribution. The mean number of colonizations for pig farm workers was far larger than either of these, at 41,777.03 [95% CI: 28,967.03, 56,831.16]. Its uncertainty distribution is plotted in Fig. 3. Thus, the number of colonizations of farm workers exceeded that of pork handlers and consumers combined by a factor of about 30. The incidence of colonization among pig farm workers constitutes 96.8% of the total risk pool.

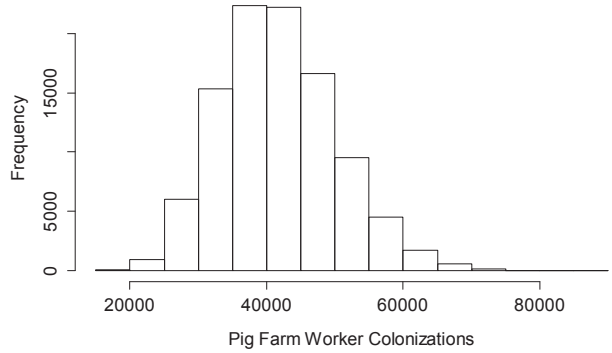

Fig. 3. Distribution of annual MRSA colonizations attributable to pigs among pig farm workers.

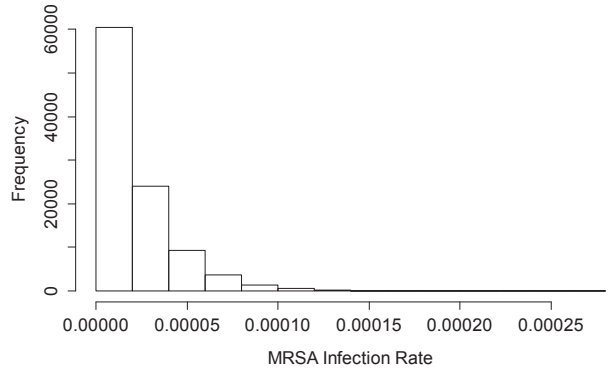

Fig. 4. Distribution of the MRSA infection rate for those colonized with pig/pork attributable MRSA.

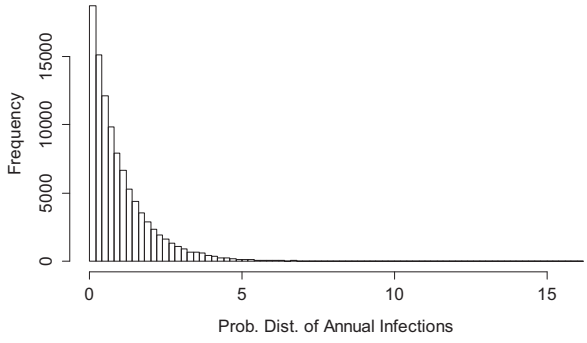

Fig. 5. Distribution of total annual U.S. MRSA infections attributable to pigs/pork.

The conditional infection rate for those colonized with pork attributable MRSA is modeled by a Beta(1, 55115) distribution as described previously. It is shown in Fig. 4. Finally, the distribution for the total annual number of pig/pork attributable MRSA infections (Equation (4)) is shown in Fig. 5. It has a mean of 1.00 [95% CI—0.05, 3.05]. If we allocate the mean according to the proportions of the

colonization risk pools, the expected total number of annual infections in U.S. pork consumers is about 0.024/yr.; in professional meat handlers, about 0.008/yr.; and in pig farm workers, about 0.968/yr.

9. DISCUSSION AND CONCLUSIONS

The size of the public health risk in the United States caused by MRSA from swine has not previously been quantified. Popular news stories have mentioned it in the context of 70,000 excess deaths per year from antibiotic-resistant superbugs.[1] Our conservative quantitative risk assessment indicates that MRSA from pigs and pork should be expected to cause no more than *about one infection per year in the U.S. population*, almost all among pig farm workers, under current conditions. To consumers (the general public) and professional meat handlers combined, swine- and pork-associated MRSA pose a risk of not more than about *one excess infection per 31 years* under current conditions. This corresponds to an average per-capita risk of about one case per 10 billion person-years (i.e., one case/(315 million people $\times$ 31 years) for the general public. Most such infections are treatable, and the excess death rate would be too small to detect. This is consistent with the historical fact that no human deaths and no serious infections have been found to have been caused among the general public or professional meat handlers by pig-associated MRSA. The fraction of all cases caused by use of antibiotics in swine is similarly undetectably small, but the finding of no statistical difference in MRSA rates between meat from hogs raised conventionally and meat from hogs raised without antibiotics[27] suggests that reducing antibiotic use on farms should not be expected to reduce the already small risk further.

We lack the comprehensive data needed to determine the applicability of these findings to the European Union. Based on the data points we do have, we suspect that risks in the EU are higher than in the United States, but still low. Herd prevalence of ST398 MRSA (25.5% EU avg.—EFSA, 2009) is higher than the 19% average for the United States we computed in Table V. We also know that ST398 MRSA prevalence on retail meats is considerably higher in the Netherlands[33] than in the United States (see studies identified in Table I). ST398 colonization rates in humans also appear to be relatively high in the European Union.[11] There are also various reports of actual ST398 infections (some of which do not distinguish "cases" between colonization and infection), while none have been reported in the United States.[7,8] On the other hand, in the Netherlands, a strict MRSA screening program is used upon hospitalization.[22]

The true risk is likely to be considerably smaller than our conservative estimates, possibly zero. We assumed that certain events, such as invasive infections resulting from ordinary colonization (from meat handling or otherwise), can occur, even though they have not been observed. The odds of their actual occurrence have become smaller as more data have accumulated, since it is Bayesian conditioning on data that moves our conservative (uniform) prior distributions leftward. In addition, modeling the dynamics of MRSA in hospitals shows that ST398 MRSA risks in hospitals are unlikely to increase dramatically in the future, as the ST398 type has a relatively low potential for spread (basic reproductive rate). Thus, a conservative upper-bound occupational risk of about one infection per pig worker per year, and a public health risk of about one infection per 31 years among the rest of the U.S. public, or about one excess case per 10 billion person-years, appears to be justified by current data. These estimates may continue to decline if further surveillance data accumulate showing no observed cases of ST398 infections among the general public.

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