The association between antibiotics and community-associated \textit{Staphylococcus aureus} colonization in the United States population

\textbf{Analysis of the National Health and Nutrition Examination Survey (NHANES)}

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\section*{Abstract}
\textit{Staphylococcus aureus} nasal colonization is a seriously opportunistic infection. However, there is a lack of research of relationship between antibiotics and \textit{S aureus} colonization in the general population. Through a cross-sectional investigation, this study intends to establish the parameters related to \textit{S aureus} nasal colonization, specifically the function antibiotics play in colonization. The key information from 2001 to 2004 was abstracted from National Health and Nutrition Examination Survey (NHANES), including information on general demographics, health care status, antibiotic prescription, diabetes, alcohol consumption, and tobacco smoke exposure. The participants colonized with methicillin-susceptible \textit{S aureus} (MSSA), or methicillin-resistant \textit{S aureus} (MRSA) were defined as the case group, and the control group was subjects without positive \textit{S aureus} colonization. Univariate and multivariate logistic regression models were used to identify the variables associated with MSSA and MRSA colonization. The records of 18,607 individuals were included, involving 13,205 cases without \textit{S aureus} colonization, 5195 cases with MSSA, and 207 cases with MRSA. In the multivariate logistic regression analysis, the risk of MSSA colonization was significantly reduced with fluoroquinolone use (75\% risk reduction, \(P = .02\)), sulfonamide use (98\% risk reduction, \(P < .01\)), tetracycline use (81\% risk reduction, \(P < .01\)) and antibiotic combination therapy (risk reduction 76\%, \(P < .01\)). Female, race and total household size were strongly associated with MSSA carriage. On the other hand, regarding MRSA colonization, fluoroquinolone use, long-term care, and former smoker were positively associated with MRSA colonization, while high income was negatively associated with MRSA colonization. More proper use of broad-spectrum antibiotics contributes to reducing MSSA colonization. Former smokers should also practice better personal hygiene to limit the possibility of MRSA colonization.

\textbf{Abbreviations:} CIs = confidence intervals, MRSA = methicillin-resistant \textit{Staphylococcus aureus}, MSSA = methicillin-susceptible \textit{Staphylococcus aureus}, NHANES = National Health and Nutrition Examination Survey, ORs = odds ratios.

\textbf{Keywords:} antibiotics, broad-spectrum antibiotics, colonization, methicillin-resistant \textit{Staphylococcus aureus}, NHANES, \textit{Staphylococcus aureus}

\section*{1. Introduction}
\textit{Staphylococcus aureus} colonization is significantly associated with many infectious illnesses, including endocarditis, periarticular infections, and postoperative infections.\textsuperscript{[1,2]} The proportions of colonization caused by methicillin-resistant \textit{S aureus} (MRSA) strains, on the other hand, has been growing during the last few decades. Every year, it kills around 19,000 inpatients in the United States.\textsuperscript{[3,4]} Furthermore, \textit{S aureus} nasal colonization highly linked to recurrent infections in individuals. Although there have been numerous research on \textit{S aureus} colonization, the majority of them have focused on patients with a specific condition (e.g., dialysis patients and HIV patients)\textsuperscript{[5,6]} or on specific special occupational groups.\textsuperscript{[7,8]} Just a few studies have investigated the characteristics of \textit{S aureus} colonization in community populations. However, the sample sizes of in these studies are too small or the respondents are not representative, preventing them from answering the research questions accurately.\textsuperscript{[9–11]}

The community prevalence of \textit{S aureus} is increasing due in large part to the colonization of \textit{S aureus}.\textsuperscript{[12,13]} Antibiotics
usages is a known factor that influences \textit{S. aureus} colonization. However, whether the antibiotic is a danger or a protective factor in \textit{S. aureus} colonization yields contradictory data.\cite{9,14-16} Most investigations have only been conducted in a few places and with unrepresentative people.\cite{11,17} Furthermore, most studies on the investigations have only been conducted in a few places and with unrepresentative people.\cite{11,17} Consequently, the role of antibiotics in \textit{S. aureus} colonization during the survey’s physical examination portion. Standard culture-based techniques were then used to assess the presence of \textit{S. aureus} in nasal swabs. Further information on the \textit{S. aureus} screen test can be found in the description of laboratory methodology on the NHANES website.\cite{18} Disk diffusion was employed to test identified \textit{S. aureus} isolates for methicillin resistance. Participants who tested negative for \textit{S. aureus} were also included in the control group.

Those who tested positive for \textit{S. aureus} but not MRSA were labeled as having methicillin-susceptible \textit{S. aureus} (MSSA). Those who tested positive for MRSA were labeled as such. In addition, no information on clinical infection status were gathered.

2.4. Covariates measurement

The demographic data comprised gender, age, education level, family income and the total number of individuals in the household as covariates for the multivariate analysis. Non-Hispanic white, Mexican, other Hispanic, non-Hispanic black, and the others were the race categories. Education was categorized as less than high school, high school, and more than high school, and with individuals under the age of 12 classified as less than high school. Income was coded dichotomously (earning <$45,000 a year). The total number of individuals in the household was represented as a continuous variable. In addition, various \textit{S. aureus} related health indicators were gathered, such as insurance status, time spent in long-term care facilities in the previous 12 months, current health status and respiratory health. The questionnaire identified the current health status (“Did you have flu, pneumonia, or ear infections that started during those 30 days?”) and was dichotomized. Respiratory health was determined from the questionnaire (“Do you usually cough on most days for 3 consecutive months or more during the year?” and “Do you bring up phlegm on most days for 3 consecutive months or more during the year?”). Furthermore, various risk factors were included as covariates in the analysis, including the use of insulin, which was modeled as a dichotomous variable. Diabetes mellitus\cite{19} was also modeled as a categorical variable involving verified diabetes, no diabetes, and borderline diabetes. Participants were divided into 3 groups: never-smokers (those who have smoked <100cig/lifetime), former smokers (having smoked >100cig/lifetime but do not currently smoke), and current smokers. All of the information was derived from self-reported questionnaires responses.

2.5. Survey weights

In order to account for the complex survey design of NHANES, the sampling weights are analyzed in accordance with the guidelines provided by the National Center for Health Statistics. We employed Mobile Examination Center survey weight to alter our estimates for each model in order to reduce the population’s ultimate unbiased.

2.6. Statistical analysis

The category variables were described using a number (percentage). Continuous variables were classified as normally distributed or non-normally distributed, using mean ± standard deviation and median (interquartile range) to define normally distributed variables and non-normally distributed variables, respectively. The chi-square test for categorical variables, the \(t\) test for normally distributed variables and the Mann–Whitney \(U\) test for non-normally distributed variables were used to make comparisons between participants without \textit{S. aureus} colonization and those with MSSA or MRSA.

The relationship between antibiotics and MRSA/MSSA colonization was analyzed by using univariate and multivariate logistic regression models. After calculating all variables using
univariate logistic regression, variables with $P$ values $<.20$ were included in the multivariate logistic regression analysis, which was then performed using backward-stepwise approaches to determine independent factors and manually remove them one by one. All factors were estimated as odds ratios (ORs) and 95% confidence intervals (CIs), and all significant associations were examined. The $P$ value of $<.05$ indicated that the difference was statistically significant. The survey package and the logistics regression models were used to create the survey design object.\[19,20\] All analyses were performed using R (version 4.1.1).

3. Result

3.1. Subject characteristics

From 2001 to 2004, the NHANES database included information on 21,161 participants. Participants who did not test positive for \textit{S aureus} or did not have prescription medication information were excluded from the research. Finally, the records of 18,607 individuals were included, involving 13,205 cases without \textit{S aureus} colonization, 5,199 cases with MSSA, and 207 cases with MRSA. Table 1 shows descriptive statistics indicating that the prevalence of MSSA and MRSA was 27.9% and 1.1%, respectively.

The characteristics of the study sample as determined by the weighted analysis approach are shown in Table 1. The participants with MSSA had a lower mean age (27.51 ± 22.34 years) than the controls (31.51 ± 24.8 years). For MSSA carriage, the total number of individuals in the household was higher than the controls (4.01 ± 1.71 vs 3.79 ± 1.74). In comparison to the control group, the MSSA group had a higher proportion of males (53.8% vs 47.0%), whites (43.4% vs 40.1%), and an income greater than 45,000 (40.3% vs 37.0%). MSSA participants had considerably lower rates of influenza, pneumonia, and ear infections than controls. It also revealed that people with MSSA had a much higher proportion of insurance than those in the control group.

In contrast, the participants with MRSA had a greater mean age (40.13 ± 29.14 years) than the mean age of the controls (31.51 ± 24.8 years). Males (44.9% vs 47.0%) and Mexican Americans (15.9% vs 24.8%) had a lower proportion of MRSA carriage than controls. Participants with MRSA had a greater rate of coughing (8.7% vs 5.5%), bringing up phlegm (12.6% vs 5.6%), long term care (5.8% vs 0.7%), diabetes mellitus (11.6% vs 5.3%), and being a former smoker (28.0% vs 14.6%) than those from the control group. Univariate analyses of MSSA/MRSA cases versus controls

There were significant differences ($P < .20$) between MSSA cases and controls in age, gender, race, education, total number of people in the household, household income, macrolides use, fluoroquinolones use, sulfonamide use, tetracycline use, lincomycin derivatives use, antibiotic combination therapy, coughing, long term care, smoking status in univariate analyses (Table 2). MRSA carriage was associated with significant variations in age, gender, race, total number of individuals in the household, fluoroquinolones use, bringing up phlegm, long term care, diabetes, and former smokers compared to the control group. Variables with substantial statistics were used to construct multivariable regression models. Multivariate analyses of MSSA cases versus controls

In the multivariate logistic analysis (Table 3), MSSA colonization was inversely correlated with advanced age ($P < .01$). Female (odds ratio [OR] = 0.69, 95% CI [0.62–0.77], $P < .01$), non-Hispanic Black (OR = 0.84, 95% CI [0.77–0.93], $P < .01$) and current smokers (OR = 0.73, 95% CI [0.65–0.81], $P < .01$) were inversely associated with having MSSA colonization. Furthermore, the risk of MSSA colonization was significantly reduced with fluoroquinolone use (risk reduction 75%, OR = 0.25, 95% CI [0.09–0.72], $P = .02$), sulfonamide use (risk reduction 98%, OR = 0.02, 95% CI [0.01–0.13], $P < .01$), tetracycline use (risk reduction 81%, OR = 0.19, 95% CI [0.08–0.46], $P < .01$), and antibiotic combination therapy (risk reduction 76%, OR = 0.24, 95% CI [0.12–0.47], $P < .01$). Factors associated with a higher risk of MSSA carriage were Other Hispanic (OR = 1.51, 95% CI [1.27–1.80], $P < .01$), Non-Hispanic White (OR = 1.29, 95% CI [1.14–1.46], $P < .01$), and the total number of individuals in the household (OR = 1.19, 95% CI [1.06–1.33], $P < .01$). The probability of MSSA carriage associated with education, income, coughing, long term care, and former smokers seen in univariable analysis was not found in multivariable analysis.

3.2. Multivariate analyses of MRSA cases versus controls

Long-term care (OR = 2.86, 95% CI [1.37–5.95], $P < .01$) and former smokers (OR = 2.11, 95% CI [1.26–3.55], $P < .01$) were factors associated with a higher risk of MRSA colonization. Participants using fluoroquinolones have a nearly 6-fold increased risk of MRSA colonization (OR = 5.90, 95% CI [1.37–25.3], $P < .01$). More than 45,000 USD in household income (OR = 0.42, 95% CI [0.27–0.67], $P < .01$) was negatively associated with MRSA (Table 3).

4. Discussion

The goal of this study is to identify the high-risk factors, for \textit{S aureus} nasal colonization, especially the connection with antibiotics, through a cross-sectional investigation. The NHANES records of 18,607 individuals met the inclusion criteria. In this study, the prevalence of MSSA was 27.9% and that of MRSA was 1.1%. MSSA colonization was found to be significantly associated with advanced age. The results indicated that females, non-Hispanic blacks, and current smokers had a lower probability of MSSA carriage. On the other hand, the risk of MSSA colonization was significantly reduced in individuals taking fluoroquinolones, sulfonamides, tetracyclines and antibiotic combination therapy, with a 74% to 98% risk reduction. Long-term care, former smokers and fluoroquinolone usage all elevated the probability of carriage, with fluoroquinolone use raising the risk of colonization by 6-fold. Surprisingly, a household income of more than 45,000 USD was found to inversely associated with MRSA colonization. While population-based research cannot be utilized to investigate causality, some of these characteristics related to MRSA colonization can be modified on an individual or societal level.

The key discovery of this analysis was the association between broad-spectrum antibiotics and MSSA colonization. The relative relevance of antibiotics in \textit{S aureus} colonization is contested in the literature. Nguyen et al found that antibiotic use to be an independent explanatory variable for \textit{S aureus} carriage, with an OR (0.69) indicating a negative connection between them.\[9\] A cross-sectional study by Chen et al\[21\] argued against this, stating that antibiotics exposure in the previous 4 weeks might be utilized to investigate causality, some of these characteristics related to MRSA colonization can be modified on an individual or societal level.

Therefore, the controlled and proper use of antibiotics is the main reason why some studies consider antibiotics to be a risk factor for colonization. In contrast, the antibiotics used by NHANES subjects were prescription medications, and the majority of them were monitored. Therefore, we conclude that the controlled and proper use of antibiotics is a protective factor against \textit{S aureus} colonization. However, due to the lack of antibiotic dose information in NHANES, we were unable to investigate them in further depth.
### Table 1

Weighted characteristics and distribution of anthropometric measures in study sample.

| Variable                        | Control   | MSSA†  | MRSA‡  | MSSA vs control | MRSA vs control |
|---------------------------------|-----------|--------|--------|-----------------|-----------------|
|                                 | n = 13205 | n = 5195 | n = 207 | P value         | P value         |
| **Gender**                      |           |        |        | .001*           | .132            |
| Male                            | 6201 (47.0) | 2793 (53.8) | 93 (44.9) |               |                 |
| Female                          | 7004 (53.0) | 2402 (46.2) | 114 (55.1) |               |                 |
| **Age**                         |           |        |        | .001*           | .439            |
| 0–20                            | 6196 (46.9) | 2828 (54.4) | 79 (38.2) |               |                 |
| 21–40                           | 2449 (18.5) | 938 (18.1) | 29 (14.0) |               |                 |
| 41–60                           | 2049 (15.5) | 739 (14.2) | 22 (10.6) |               |                 |
| >60                             | 2511 (19.0) | 690 (13.3) | 77 (37.2) |               |                 |
| **Race**                        |           |        |        | .001*           | .316            |
| Mexican American                | 3334 (25.2) | 1287 (24.8) | 33 (15.9) |               |                 |
| Other Hispanic                  | 471 (3.6) | 265 (5.1) | 2 (1.0) |               |                 |
| White§                          | 5291 (40.1) | 2253 (43.4) | 102 (49.3) |               |                 |
| Black||                         | 3649 (26.9) | 1195 (23.0) | 63 (30.4) |               |                 |
| Other race¶                     | 660 (4.2) | 198 (3.8) | 7 (3.4) |               |                 |
| **Education**                   |           |        |        | .002            | .426            |
| No high school diploma          | 6057 (45.9) | 2753 (53.0) | 92 (44.4) |               |                 |
| High school diploma             | 1967 (14.9) | 694 (13.4) | 30 (14.5) |               |                 |
| >High school diploma            | 3315 (25.1) | 1239 (23.8) | 54 (26.1) |               |                 |
| **Number of household**         |           |        |        | .001*           | .257            |
| 1–3                             | 6094 (46.1) | 2033 (39.1) | 121 (58.5) |               |                 |
| ≥4                              | 7111 (53.9) | 3162 (60.9) | 86 (41.5) |               |                 |
| **Household income (USD)**      |           |        |        | .002            | .426            |
| <45,000                         | 7321 (55.4) | 2734 (52.6) | 152 (73.4) |               |                 |
| ≥45,000                         | 4886 (37.0) | 2095 (40.3) | 42 (20.3) |               |                 |
| **Antibiotics class**           |           |        |        |                 |                 |
| No medicine                     | 7942 (60.1) | 3290 (63.3) | 86 (41.5) |               |                 |
| Cephalosporins                  | 100 (0.8) | 37 (0.7) | 0 (0.0) |               |                 |
| Macrolides                      | 87 (0.7) | 15 (0.3) | 0 (0.0) |               |                 |
| Penicillins                     | 309 (2.3) | 125 (2.4) | 5 (2.4) |               |                 |
| Fluoroquinolones                | 36 (0.3) | 5 (0.1) | 3 (1.4) |               |                 |
| Sulfonamides                    | 33 (0.2) | 1 (0.0) | 0 (0.0) |               |                 |
| Tetracyclines                   | 94 (0.7) | 9 (0.2) | 0 (0.0) |               |                 |
| Aminoglycosides                 | 3 (0.0) | 2 (0.0) | 1 (0.5) |               |                 |
| Lincomycin derivatives          | 18 (0.1) | 2 (0.0) | 0 (0.0) |               |                 |
| Antibiotic combination therapy  | 82 (0.6) | 11 (0.2) | 2 (1.0) |               |                 |
| Antibiotic unspecified          | 49 (0.4) | 15 (0.3) | 0 (0.0) |               |                 |
| Non-antibiotics drugs           | 4452 (33.7) | 1683 (32.4) | 110 (53.1) |               |                 |
| **Coughing**                    |           |        |        | .125            | .090            |
| No                              | 9389 (71.1) | 3575 (68.8) | 139 (67.1) |               |                 |
| Yes                             | 726 (5.5) | 217 (4.2) | 18 (8.7) |               |                 |
| **Phlegm**                      |           |        |        | .115            | .161            |
| No                              | 9379 (71.0) | 3554 (68.4) | 131 (63.3) |               |                 |
| Yes                             | 737 (5.6) | 237 (4.6) | 26 (12.6) |               |                 |
| **Current health status**       |           |        |        | .016*           | .073            |
| No                              | 11592 (87.8) | 4625 (89.0) | 180 (87.0) |               |                 |
| Yes                             | 794 (6.0) | 257 (4.9) | 11 (5.3) |               |                 |
| **Insurance**                   |           |        |        | .041*           | .129            |
| No                              | 9899 (75.0) | 3904 (75.1) | 164 (79.2) |               |                 |
| Yes                             | 684 (5.2) | 288 (5.5) | 13 (6.3) |               |                 |
| **Long-term care**              |           |        |        | .052            | .169            |
| No                              | 13114 (99.3) | 5174 (99.6) | 195 (94.2) |               |                 |
| Yes                             | 90 (0.7) | 21 (0.4) | 12 (5.8) |               |                 |
| **Diabetes mellitus**           |           |        |        | .013*           | .200            |
| No                              | 12394 (93.9) | 4903 (94.4) | 179 (86.5) |               |                 |
| Yes                             | 110 (0.8) | 34 (0.7) | 4 (1.9) |               |                 |
| **Insulin**                     |           |        |        | .008*           | .053            |
| No                              | 13028 (98.7) | 5128 (98.7) | 202 (97.6) |               |                 |
| Yes                             | 177 (1.3) | 67 (1.3) | 5 (2.4) |               |                 |
| **Alcohol consumption (drink/yr)** |         |        |        | .151            | .078            |
| <12                             | 2078 (15.7) | 674 (13.0) | 42 (20.3) |               |                 |
| ≥12                             | 4436 (33.6) | 1510 (29.1) | 74 (35.7) |               |                 |
| **Smoking status**              |           |        |        | .147            | .389            |

(Continued)
Another interesting discovery is the relationship between overall household size and MSSA colonization. Families have been demonstrated to act as community reservoirs of *S. aureus*. Our findings are consistent prior research that suggests MSSA carriage may be caused by living in more crowded conditions, which increases the chance of *S. aureus* transmission. Smoking is also found to be a substantial predictor of MSSA. We discovered that the probability of MSSA carriage reduces with age (OR value decreases consistently), which is consistent with the finding of earlier investigations.

In our study, current smoking was found to be inversely related to the risk of MSSA colonization. Other investigations have observed similar findings, with the hypothesis that cigarettes have bactericidal activity and increase hypoxia-related immunoreactivity. Furthermore, the risk of MSSA carriage varies by race, with whites and other Hispanics being more at risk than blacks. We cannot assume that race is connected with limited access to healthcare because race cannot be used as a proxy for socioeconomic situations and no statistical differences were detected at the education and income levels.

We found no consistency in risk factors for MRSA and MSSA colonization in community populations. However, characteristics, smoking and quinolone use, were found to be associated in different directions with MRSA and MSSA colonization. Tobacco exposure, in particular, reduces the growth of colonizing bacteria, which could explain why being exposed to tobacco is a protective factor for MSSA.

Simultaneously, tobacco smoking causes DNA damage to the induced *S. aureus* in the nasal cavity, hastening the pace of mutation and eventually leading to antibiotic resistance. Former smokers may become factors for MRSA colonization due to a lack of tobacco suppression and MRSA being the primary colonizing bacteria in the nasal cavity. During this time, tobacco exposure-induced impairment of mucociliary clearance mechanisms in the sinus epithelium, as well as down-regulation of local immunological responses, both enhance MRSA colonization and subsequent reinfection. Additionally, the usage of fluoroquinolones was strongly associated with MRSA but negatively associated with MSSA colonization. Previous research has found that using fluoroquinolones increases the probability of MRSA colonization or infection when compared to no *S. aureus* isolation. It has been proposed that due to their excellent tissue diffusion, fluoroquinolones can encourage the proliferation and selection of MRSA by removing fluoroquinolone-sensitive microbes such as MSSA. However, due to only 3 subjects using fluoroquinolones in the MRSA group, this has to be interpreted with caution.

Furthermore, we discovered 2 risk factors for MRSA colonization: long-term care and higher income. Subjects in long-term care facilities have previously been found to have higher MRSA colonization, a risk factor that may be a sign of disease severity and suggests the probability of bacterial transmission through caregivers. Economic pressures increased the likelihood of taking antibiotics in Sweden, whereas in the United Kingdom, higher rates of antibiotic prescribing were reported in primary care in poorer areas. Although we cannot conclude that income increases or decrease the odds of antibiotic base on this study, income was substantially connected with MRSA and high income was a protective factor for MRSA. This could be due to the relationship between income and the level of care.

A limitation of this study is that the demographic data from NHANES was obtained 15 years ago. Despite the fact that it was the only national data available, it is possible the epidemiological changes may not reflect *S. aureus*. Second, different ways of evaluating of *S. aureus* colonization, such as study design, control group definition and population, may have an impact on the evaluation of *S. aureus* colonization. For example, we may overstate the importance and risk of antibiotics in the carriage of MRSA if we utilize MSSA as a control group. Third, non-antibiotic medicines have the potential to be relevant to MRSA carriage. Unfortunately, the researchers were unable to classify non-antibiotic medications in order to determine their significance in MRSA colonization. The major disadvantage of this study is that the cross-sectional data did not allow for a casual analysis. It is uncertain if long-term antibiotics have a higher effect on *S. aureus* colonization due to a lack of evidence on the duration and dose of antibiotics usage. Further studies are needed to determine the relationship between *S. aureus* and the duration and dose of antibiotic use in the general population.

### Table 1

| Variable                | Control | MSSA | MRSA          |
|-------------------------|---------|------|---------------|
| Never-smokers           | 5582 (42.3) | 2289 (44.1) | 64 (30.9) |
| Former smokers          | 1922 (14.6) | 655 (12.6) | 58 (28.0) |
| Current smokers         | 2373 (18.0) | 754 (14.5) | 32 (15.5) |

MSSA vs control | MRSA vs control

| P value | P value |
|---------|---------|

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### 5. Conclusion

This is the first study to look at the connection between antibiotics and *S. aureus* and MRSA colonization in a nationally representative cohort of patients. It demonstrates a low national prevalence of MRSA colonization but a widespread national prevalence of MSSA. Our findings indicated that broad-spectrum antibiotics were positively related to MSSA colonization. Antibiotics should be used in a controlled and suitable manner to reduce *S. aureus* colonization. Physicians should be aware of the likelihood of MRSA colonization and the possibility of infection in patients who have used fluoroquinolone in the last 30 days. Former smokers should also practice better personal hygiene to limit the possibility of MRSA colonization.
Table 2
Univariate analyses of MSSA/MRSA cases versus controls by weighted.

| Variable                      | Control vs MSSA† | Control vs MRSA‡ |
|-------------------------------|------------------|-----------------|
|                               | OR (95% CI)      | P value         | OR (95% CI)      | P value         |
| Gender                        |                  |                 |                  |                 |
| Female                        | 0.72 (0.65–0.79) | <.01*           | 1.31 (0.94–1.82) | .13*            |
| Age                           |                  |                 |                  |                 |
| 0–20                          | Reference        |                 | Reference        |                 |
| 21–40                         | 0.76 (0.69–0.83) | <.01*           | 0.90 (0.59–1.38) | .65             |
| 41–60                         | 0.73 (0.65–0.84) | <.01*           | 0.84 (0.40–1.77) | .66             |
| >60                           | 0.55 (0.49–0.61) | <.01*           | 2.48 (1.43–4.29) | <.01*           |
| Race                          |                  |                 |                  |                 |
| Mexican American              | Reference        |                 | Reference        |                 |
| Other Hispanic                | 1.41 (1.18–1.67) | <.01*           | 0.27 (0.05–1.54) | .15*            |
| White                         | 1.12 (0.99–1.26) | .08*            | 1.98 (0.90–4.39) | .10*            |
| Black                         | 0.78 (0.71–0.87) | <.01*           | 1.86 (0.89–3.90) | .11*            |
| Other Race                    | 0.89 (0.69–1.14) | .37             | 1.27 (0.44–3.65) | .66             |
| Education                     |                  |                 |                  |                 |
| <High School Diploma          | Reference        |                 | Reference        |                 |
| High School Diploma           | 0.74 (0.66–0.83) | <.01*           | 1.02 (0.73–1.42) | .91             |
| >High School Diploma          | 0.83 (0.76–0.92) | <.01*           | 0.87 (0.57–1.33) | .54             |
| Number of Household           |                  |                 |                  |                 |
| 1–4                           | 1.33 (1.20–1.47) | <.01*           | 0.59 (0.34–1.03) | .07*            |
| ≥4                            | Reference        |                 | Reference        |                 |
| Household income (USD)        |                  |                 |                  |                 |
| <45,000                       | Reference        |                 | Reference        |                 |
| ≥45,000                       | 1.17 (1.06–1.29) | <.01*           | 0.42 (0.26–0.66) | <.01*           |
| Prescription medicine         |                  |                 |                  |                 |
| No medicine                   | Reference        |                 | Reference        |                 |
| Cephalosporins                | 0.88 (0.58–1.32) | .53             | 0               |                 |
| Macrolides                    | 0.53 (0.30–0.91) | .03*            | 0               |                 |
| Penicillins                   | 1.09 (0.80–1.48) | .59             | 1.61 (0.48–5.35) | .45             |
| Fluoroquinolones              | 0.07 (0.02–0.30) | <.01*           | 7.14 (1.74–29.27) | .01*           |
| Sulfonamides                  | 0.08 (0.03–0.21) | <.01*           | 0               |                 |
| Tetracyclines                 | 0.20 (0.08–0.46) | <.01*           | 0               |                 |
| Aminoglycosides               | 0.89 (0.06–14.29) | .93             | 5.81 (0.50–67.09) | .18             |
| Lincomycin derivatives        | 0.16 (0.03–0.99) | .06*            | 0               |                 |
| Antibiotic combination therapy| 0.15 (0.06–0.41) | <.01*           | 1.76 (0.23–13.52) | .50             |
| Antibiotics unspecified       | 0.52 (0.24–1.14) | .12             | 0               |                 |
| Non-antibiotics drugs         | 0.93 (0.85–1.01) | .09*            | 2.55 (1.78–3.67) | <.01*           |
| Coughing                      |                  |                 |                  |                 |
| Yes                           | 0.78 (0.62–0.99) | .05*            | 1.34 (0.73–2.45) | .35             |
| Phlegm                        |                  |                 |                  |                 |
| Yes                           | 0.90 (0.72–1.12) | .35             | 1.72 (0.97–3.04) | .07*            |
| Current health status         |                  |                 |                  |                 |
| Yes                           | 0.96 (0.78–1.17) | .68             | 1.34 (0.49–3.66) | .57             |
| Insurance                     |                  |                 |                  |                 |
| Yes                           | 1.05 (0.89–1.25) | .58             | 1.66 (0.78–3.54) | .20             |
| Long-term care                |                  |                 |                  |                 |
| Yes                           | 0.48 (0.25–0.90) | .03*            | 4.33 (2.02–9.29) | <.01*           |
| Diabetes mellitus             |                  |                 |                  |                 |
| No                             | Reference        |                 | Reference        |                 |
| Borderline                    | 1.12 (0.60–2.06) | .73             | 2.62 (0.91–7.53) | .09*            |
| Yes                           | 0.97 (0.75–1.24) | .80             | 1.94 (1.14–3.31) | .02*            |
| Insulin                       |                  |                 |                  |                 |
| Yes                            | 1.08 (0.69–1.68) | .75             | 1.53 (0.53–4.45) | .44             |
| Alcohol consumption (drink/yr)|                  |                 |                  |                 |
| <12                           | Reference        |                 | Reference        |                 |
| ≥12                           | 1.06 (0.92–1.23) | .42             | 0.86 (0.52–1.41) | .55             |
| Smoking status                |                  |                 |                  |                 |
| Never-smokers                 | Reference        |                 | Reference        |                 |
| Former smokers                | 0.90 (0.79–1.03) | .12*            | 2.58 (1.53–4.36) | <.01*           |
| Current smokers               | 0.78 (0.70–0.86) | <.01*           | 1.13 (0.62–2.06) | .70             |

CI = confidence interval, OR = odds ratio.
†MSSA - Methicillin-susceptible Staphylococcus aureus.
‡MRSA - Methicillin-resistant Staphylococcus aureus.
§Non-Hispanic White.
||Non-Hispanic Black.
*Other Race - Including Multi-Racial.
#The total number of people in the household.
**Coughing over 3 months period.
###Bring up phlegm over 3 months period.
####having flu, pneumonia, or ear infections that started during those 30 days.
*P < .20.
### Table 3
Multivariate analyses of MSSA/MRSA cases versus controls.

| Variable                        | Control vs MSSA | Control vs MRSA |
|--------------------------------|-----------------|-----------------|
|                                | Unadjusted model | Final adjusted model | Unadjusted model | Final adjusted model |
|                                | OR (95% CI)      | P value          | OR (95% CI)      | P value          |
| Gender                         |                 |                  |                 |                  |
| Female                         | 0.69 (0.62–0.77) | <.01*            | 0.69 (0.62–0.77) | <.01*            |
| Male                           | 1.00 (0.91–1.10) |                  | 1.00 (0.91–1.10) |                  |
| Age                            |                 |                  |                 |                  |
| 0–20                           | Reference       | Reference        | Reference       | Reference        |
| 21–40                          | 0.78 (0.66–0.93) | .01*             | 0.82 (0.72–0.93) | .01*             |
| 41–60                          | 0.71 (0.62–0.83) | <.01*            | 0.74 (0.65–0.85) | <.01*            |
| >60                            | 0.54 (0.45–0.64) | <.01*            | 0.55 (0.47–0.63) | <.01*            |
| Race                           |                 |                  |                 |                  |
| Mexican American               | Reference       | Reference        | Reference       | Reference        |
| Other Hispanic                 | 1.50 (1.25–1.80) | <.01*            | 1.51 (1.27–1.80) | <.01*            |
| White (1)                      | 1.27 (1.11–1.45) | <.01*            | 1.29 (1.14–1.46) | <.01*            |
| Black (2)                      | 0.82 (0.74–0.91) | <.01*            | 0.84 (0.77–0.93) | <.01*            |
| Other Race (3)                 | 0.92 (0.71–1.19) | .53              | 0.95 (0.73–1.22) | .67              |
| Education (%                   |                 |                  |                 |                  |
| <High School Diploma           | Reference       | Reference        | Reference       | Reference        |
| High School Diploma            | 1.00 (0.86–1.17) | .99              |                  |                  |
| >High School Diploma           | 1.09 (0.92–1.28) | .32              |                  |                  |
| Number of Household (4)        |                 |                  |                 |                  |
| 1–3                            | 1.18 (1.05–1.32) | .01              | 1.19 (1.06–1.33) | .01              |
| ≥4                            | 0.90 (0.84–1.00) | .34              | 0.90 (0.84–1.00) | .34              |
| Household income (USD)         |                 |                  |                 |                  |
| <45,000                        | Reference       | Reference        | Reference       | Reference        |
| ≥45,000                        | 1.01 (0.91–1.12) | .89              | 0.90 (0.84–1.00) | .90              |
| Prescription medicine (%)      |                 |                  |                 |                  |
| No medicine                    | Reference       | Reference        | Reference       | Reference        |
| Cephalosporins                 | 0.90 (0.58–1.39) | .63              |                  |                  |
| Macrolides                     | 0.56 (0.31–0.99) | .05              |                  |                  |
| Penicillins                    | 1.02 (0.73–1.41) | .92              |                  |                  |
| Quinolones                     | 0.26 (0.09–0.76) | .02*             | 0.25 (0.09–0.72) | .02*             |
| Ceftriaxone                     | 0.02 (0.01–0.13) | <.01*            | 0.02 (0.01–0.13) | <.01*            |
| Tetracyclines                  | 0.19 (0.08–0.46) | <.01*            | 0.19 (0.08–0.46) | <.01*            |
| Aminoglycosides                | 0.50 (0.03–9.77) | .65              |                  |                  |
| Lincomycin derivatives         | 0.19 (0.03–1.31) | .10              |                  |                  |
| Antibiotic combination therapy | 0.24 (0.12–0.48) | <.01*            | 0.24 (0.12–0.47) | <.01*            |
| Antibiotics unspecified        | 0.81 (0.38–1.70) | .58              |                  |                  |
| Non-antibiotics drugs          | 1.16 (1.04–1.29) | .01*             | 1.16 (1.03–1.29) | .02*             |
| Coughing                       |                  |                  |                  |                  |
| Yes                            | 0.85 (0.67–1.07) | .17              |                  |                  |
| Long-term care (%)             |                  |                  |                  |                  |
| Yes                            | 0.61 (0.33–1.12) | .12              |                  |                  |
| Former smokers                 |                  |                  |                  |                  |
| Yes                            | 2.15 (0.99–4.65) | .06              |                  |                  |
| Former smokers                 | 0.93 (0.81–1.08) | .34              |                  |                  |
| Current smokers                | 0.75 (0.68–0.84) | <.01*            | 0.73 (0.65–0.81) | <.01*            |
| Diabetes mellitus (%)          |                  |                  |                  |                  |
| No                             |                  |                  |                  |                  |
| Borderline                     | Reference        |                  |                  |                  |
| Yes                            | 1.48 (0.45–4.85) | .52              |                  |                  |

CI = confidence interval, OR = odds ratio.

1. Unadjusted model, multivariable full models correspond to models including all the variables with P value < 0.20 in univariate analyses.
2. Final adjusted models for gender, age, race, the total number of people in the household, prescription medicine and smoking status, which correspond to models including all the remaining variables showing significant OR estimates after manual backward-stepwise selections.
3. Final adjusted models for race, household income, fluoroquinolones, long-term care and former smokers, which correspond to models including all the remaining variables showing significant OR estimates after manual backward-stepwise selections.

*P < .05.

**The total number of people in the household.
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