Risk Factors for Resistance to Antimicrobial Agents among Nursing Home Residents

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The authors prospectively collected data on exposure to antimicrobial agents and susceptibility patterns among all clinical isolates of bacteria taken from 9,156 residents of 50 nursing homes in Canada and the United States in 1998–1999. Exposure to antimicrobial agents was measured during the 10 weeks prior to detection of targeted resistant bacteria in residents and compared with antibiotic exposure during a 10-week interval in individuals with sensitive organisms. These main effects were adjusted for infection-control and staffing covariates using multiple logistic regression modeling. Increased staffing of nursing homes with registered nurses (adjusted odds ratio (OR) = 0.79 (95% confidence interval (CI): 0.72, 0.87) per registered nurse per 100 resident-days) and use of antibacterial soap (adjusted OR = 0.40, 95% CI: 0.18, 0.90) were associated with reduced risk of methicillin-resistant Staphylococcus aureus in nursing home residents. An increase in the number of hand-washing sinks per 100 residents was shown to reduce the risk of trimethoprim-sulfamethoxazole (TMP/SMX)-resistant Enterobacteriaceae (adjusted OR = 0.94, 95% CI: 0.90, 0.98). Exposure to TMP-SMX and exposure to fluoroquinolones were significant risk factors for isolation of TMP-SMX-resistant Enterobacteriaceae (adjusted OR = 1.14, 95% CI: 1.06, 1.22) and fluoroquinolone-resistant Enterobacteriaceae (adjusted OR = 1.08, 95% CI: 1.04, 1.11), respectively. These findings suggest that increased staffing, more hand-washing sinks, and use of antimicrobial soap may reduce resistance to antimicrobial agents in long-term care facilities.

antibiotics; drug resistance, microbial; nursing homes

Abbreviations: CI, confidence interval; MRSA, methicillin-resistant Staphylococcus aureus; OR, odds ratio; TMP-SMX, trimethoprim-sulfamethoxazole.

There is increasing concern about the emergence of resistance to antimicrobial agents (antimicrobials) in long-term care facilities (1, 2). Use of antimicrobial agents in these settings is intense. It is estimated that two to four million courses of antibiotics are prescribed for residents of US nursing homes annually (3). As a result, 50–75 percent of residents in US nursing homes are exposed to at least one course of antibiotics over a 12-month period (4–8). Numerous reports of antimicrobial-resistant organisms among residents of long-term care facilities exist (9–17). Despite the frequent use of antimicrobial agents and reports of resistance to antimicrobial agents, risk factors for acquisition of antimicrobial-resistant bacteria among residents of long-term care facilities in the non-outbreak setting are not

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well defined (18, 19). Studies implicating use of antimicrobial agents as a risk factor generally either have been limited to outbreak settings, have been conducted in single facilities, or have not considered the effect of duration or dosage of antibiotic exposure (16, 17, 20–22). Previous studies have emphasized resident characteristics as risk factors for infection with antimicrobial-resistant bacteria, including underlying illness, decubitus ulcers, and use of urinary catheters or feeding tubes (23–25). However, less is known about risk factors at the facility level.

Antimicrobial-resistant bacteria can spread from person to person by handborne transmission. Therefore, knowing the effect of a long-term care facility’s infrastructure for hand hygiene, such as the availability of hand-washing sinks or the use of antibacterial soaps, may lead to interventions to help reduce the transmission of resistance to antimicrobial agents. Given recent reductions in staffing in long-term care facilities (26), it is particularly important to assess whether a reduced level of staffing is associated with an increased prevalence of antimicrobial-resistant bacteria in nursing home settings.

We conducted a study to determine antimicrobial and institutional risk factors for the isolation of antimicrobial-resistant bacteria from residents of nursing homes in Canada and the United States.

MATERIALS AND METHODS

Nursing homes

Nursing homes in four Canadian provinces (Ontario, Manitoba, Saskatchewan, and Alberta) and four adjacent US states (Michigan, Minnesota, North Dakota, and Montana) were invited to participate in the study. For the purposes of this study, a nursing home was defined as a facility where all residents received at least 90 minutes of direct nursing care per day. In the United States, the participating homes would be considered skilled nursing facilities. To enhance representation of the majority of nursing homes in North America, we ensured that none of these homes were affiliated with acute-care hospitals, universities, or other health care facilities. Veterans’ facilities and rehabilitation facilities were excluded. Restricting the study sample to freestanding, community-based facilities allowed for the study of residents who might be at similar baseline risks (on the basis of similar demographic characteristics and comorbidity) of having antibiotic-resistant isolates. To allow for potentially higher rates of antibiotic-resistant bacteria, we stipulated that only nursing homes with 100 or more beds were eligible for the study. It was anticipated that larger homes would have more transfers from acute-care facilities, with a greater likelihood of the introduction (and therefore spread) of antibiotic-resistant bacteria. With the exception of Ontario, Michigan, and Minnesota, where there were over 100 eligible facilities, all such nursing homes in the provinces or states were invited to participate. Twenty-five randomly sampled nursing homes in Ontario, Michigan, and Minnesota were also selected. Prior to the study, a questionnaire was sent to the microbiology laboratories servicing the nursing homes to ensure that methods for the detection of antibiotic-resistant bacteria were standardized according to the National Committee for Clinical Laboratory Standards (27).

This study was approved by the ethics review board of Hamilton Health Sciences and McMaster University.

Data collection

Data about nursing home size (number of beds), admission rates, resident characteristics at the facility level (use of feeding tubes, use of urinary catheters, proportion of residents confined to a bed or wheelchair), staffing (numbers of health care aides, nurses, and physicians), and infrastructure for hand-washing (number of hand-washing sinks, type of soap used) were collected using a questionnaire sent to each study nursing home. No data on individual-level factors such as functional status, severity of illness, comorbidity, the presence of roommates, or medical devices (urinary catheters or feeding tubes) were collected. Each nursing home’s infection control practitioner completed the data collection form. Since entry into the study was staggered, the data collection period began on February 1, 1998, and ended on June 30, 1999. Data were collected prospectively over a 12-month period.

The name, duration, dose, and route of all antibiotics prescribed were recorded by the nursing home’s infection control practitioner or designate. All nursing homes had service provided by a community pharmacy. For verification of accuracy, records from the pharmacy affiliated with the nursing home were obtained quarterly and reviewed. Only systemic antimicrobial agents administered within the nursing home were assessed.

All clinical bacterial culture results, including the site from which the organism was obtained, the name of the bacterium, and the susceptibility results, were obtained. Since all microbiology results from requested tests are returned to the nursing homes, complete information on bacterial cultures sent was obtained. To minimize biased sampling of resistant bacteria versus sensitive bacteria, we included only cultures sent for signs of clinical infection. However, none of the participating nursing homes routinely performed surveillance cultures—that is, cultures for the purpose of detecting resistant bacteria—at the time of the study.

Both antibiotic use and susceptibility results were linked to a unique identifier for each nursing home resident which consisted of a code for the facility, the resident’s initials, the unit, and the room number. These data were used to analyze the relations between the following five groups of resistant bacteria and certain target antimicrobial agents: trimethoprim-sulfamethoxazole (TMP-SMX)-resistant Enterobacteriaceae and TMP-SMX; fluoroquinolone-resistant Enterobacteriaceae and fluoroquinolones; fluoroquinolone-resistant *Pseudomonas aeruginosa* and fluoroquinolones; methicillin-resistant *Staphylococcus aureus* (MRSA) and fluoroquinolones; and MRSA and penicillins. We performed manual verification to ensure that repeat isolates (the same organism and antibiogram being isolated within 2 weeks of the first isolation) were not included in the analysis.
Statistical analysis

We sought to compare antibiotic exposure among nursing home residents from whom antimicrobial-resistant bacteria were isolated with exposure among residents from whom susceptible cultures were obtained. For example, TMP-SMX use in residents with TMP-SMX-resistant Enterobacteriaceae was compared with TMP-SMX use in residents with TMP-SMX-sensitive Enterobacteriaceae. The amount of antibiotic used was calculated using defined daily dosages, where one defined daily dose is equivalent to the standard amount of antibiotic in a typical prescription (28). Both dosage and duration of antibiotic exposure were taken into account. For each resistant bacterium and target antimicrobial agent, an analysis was performed by measuring antibiotic exposure (in defined daily doses) during the 10 weeks prior to detection of the resistant bacteria in residents and comparing this with antibiotic exposure during a 10-week interval in individuals with sensitive organisms detected. In the absence of any evidence defining an optimal period for assessment of antibiotic exposures, 10 weeks was selected by the consensus opinion of five infectious diseases specialists who have research expertise in the field of resistance to antimicrobial agents. Odds ratios associated with one defined daily dose per 100 resident-days were calculated using logistic regression. These odds ratios represented the risk of nursing home residents having clinical isolates of resistant organisms as compared with antibiotic-sensitive organisms.

Using logistic regression, we constructed multivariable models for the antibiotic exposures described above. Nursing home variables, including number of occupied beds, staffing characteristics (limited to those staff providing direct resident care), hand-washing characteristics, use of intravenous medications, and rates of new admissions, admissions from acute care, and returning admissions from acute care, were considered as covariates in the multivariable models. Univariate analysis was performed first. Variables for which the likelihood ratio test had a p value of less than 0.2 were selected, and the odds ratio associated with a change of one standard deviation in the variable was calculated. Covariates with an odds ratio greater than 1.1 or less than 0.9 were retained as candidates for multivariable analysis. Using forward selection and a cutoff of p < 0.05 for retention of variables, we built multivariable models in which covariates were added to antibiotic exposure. For assessment of the effect of antimicrobial exposure when adjusted for other factors, variables for these antimicrobial exposures were forced into their respective models. Facility-level antimicrobial use—that is, usage over the 12-month study period in each study home (measured as defined daily doses per 100 resident-days)—was also considered as a covariate. All data entry and analysis was performed using SAS software, versions 6.0 and 7.0 (SAS Institute, Inc., Cary, North Carolina).

RESULTS

Characteristics of residents and nursing homes

Fifty of the 218 nursing homes invited to participate were enrolled in the study. These included seven facilities in Ontario, 11 in Manitoba, nine in Saskatchewan, six in Alberta, five in Michigan, three in Minnesota, six in North Dakota, and three in Montana. Participating facilities were distributed between urban (18 homes), semirural (18 homes), and rural (14 homes) locations. The mean size (number of occupied beds) of the nursing homes was 185 beds (range, 100–490 beds). There was no difference in size between Canadian and US nursing homes (191 beds (standard deviation 75) vs. 168 beds (standard deviation 95), p = 0.37). Participating facilities had significantly more beds than nonparticipating facilities (185 beds (standard deviation 82) vs. 158 beds (standard deviation 67), p = 0.04).

There were 9,156 residents in the study homes at baseline, 47 percent of whom were either bed-bound or confined to a wheelchair. Four percent of residents had indwelling urinary catheters, and 3 percent had feeding tubes. There was no significant difference between the proportion of residents in Canadian homes and the proportion of residents in US homes who had urinary catheters (p = 0.85) or feeding tubes (p = 0.55). The median value for the average length of stay of residents in the 50 study homes, based on data from 5 years prior to the beginning of the study, was 2.2 years. The average length of stay was 2.5 years.

Data on factors pertaining to staffing and hand-washing are shown in table 1. Infection control duties were performed by practitioners or designated staff a mean of 4.9 hours per week per 100 residents (standard deviation 6.4). Thirty-six (72 percent) homes used antibacterial soap, and in 27 (54 percent) homes, antibacterial soap was used by staff but not by residents.

Use of antibiotics

Over a 1-year period, 15,878 courses of antibiotics were prescribed to 7,233 of the 9,156 residents (79 percent); residents who received antibiotics were prescribed an average of 2.2 courses of antibiotics. Twenty-one percent (n = 1,923) of residents in this study received no systemic antibiotics. The rate of antibiotic use in the 50 facilities ranged from 1.9 courses to 14.9 courses (10.8–95.5 defined daily doses per 1,000 resident-days). There was significantly more antibiotic usage in US nursing homes than in Canadian homes (6.0 courses vs. 4.6 courses per 1,000 resident-days, p = 0.04). This difference was similar when antibiotics were measured in defined daily dosages (43.8 defined daily doses per 1,000 resident-days vs. 32.9 defined daily doses, p = 0.03). Seventy-nine percent of residents in study facilities received at least one course of antibiotics. Ninety-three percent of antibiotics were prescribed orally, 4 percent by intramuscular injection, 2 percent by feeding tubes, and 1 percent parenterally. Cephalosporins (first-, second-, third-, and fourth-generation agents) accounted for 24 percent, fluoroquinolones (ciprofloxacin, norfloxacin, ofloxacin, levofloxacin, trovafloxacin, and grepafloxacin) for 20 percent, penicillins (amoxicillin, ampicillin, cloxacillin, piperacillin, ticarcillin, penicillin V, penicillin G, and clavulanic acid) for 17 percent, TMP-SMX for 16 percent, and macrolides (erythromycin, azithromycin, and clarithromycin) for 8 percent of antimicrobial agents prescribed. The remaining 15 percent of
Antimicrobial agents included aminoglycosides, carbapenems, glycopeptides, lincosamides, and tetracyclines.

Microbiology results

Data on the clinical isolates obtained in the study homes are summarized in table 2. There were 2,478 isolates of Enterobacteriaceae, 339 isolates of P. aeruginosa, and 353 isolates of S. aureus. Of the Enterobacteriaceae isolates, 54 percent were Escherichia coli, 20 percent were Proteus mirabilis, and 12 percent were Klebsiella pneumoniae. Ninety-one percent of Enterobacteriaceae were urinary isolates; 53 percent of P. aeruginosa were urinary isolates, and 23 percent of P. aeruginosa were from wounds. Only two surveillance cultures were received (one rectal swab and one nasal swab, both for MRSA), and these were not included in the analysis. S. aureus cultures were most commonly isolated from wounds (32 percent) and urine (16 percent).

Of the Enterobacteriaceae tested, 14 percent were resistant to TMP/SMX, 4 percent were resistant to fluoroquinolones, and 3 percent were resistant to gentamicin. The proportion of Enterobacteriaceae resistant to TMP/SMX in the study nursing homes ranged from 0 to 33 percent; the median was 11 percent. The proportion of fluoroquinolone-resistant Enterobacteriaceae ranged from 0 to 19 percent; the median was 8 percent. For Enterobacteriaceae resistant to gentamicin, the percentages ranged from 0 to 14 (with a median of 4 percent in homes where it was detected). Nineteen percent of P. aeruginosa were resistant to fluoroquinolones, with the

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Bacteria</th>
<th>No. of isolates</th>
<th>Isolates tested for resistance</th>
<th>No. of resistant isolates</th>
<th>% of bacteria tested that were resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TMP-SMX†</td>
<td>Enterobacteriaceae</td>
<td>2,478</td>
<td>2,210</td>
<td>89</td>
<td>302</td>
</tr>
<tr>
<td>Methicillin</td>
<td>Staphylococcus aureus</td>
<td>353</td>
<td>353</td>
<td>100</td>
<td>115</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>Enterobacteriaceae</td>
<td>2,478</td>
<td>1,992</td>
<td>80</td>
<td>82</td>
</tr>
<tr>
<td></td>
<td>Pseudomonas aeruginosa</td>
<td>339</td>
<td>316</td>
<td>93</td>
<td>61</td>
</tr>
</tbody>
</table>

* Bacterial cultures were collected from nursing home residents over a 12-month period from February 1998 to June 1999 in each of 50 nursing homes.
† TMP-SMX, trimethoprim-sulfamethoxazole.
TABLE 3. Association between antimicrobial exposure and resistance to antimicrobial agents and effect of institutional factors in 50 nursing homes in the United States and Canada, 1998–1999*

<table>
<thead>
<tr>
<th>Antimicrobial-resistant bacteria</th>
<th>Variables kept in the multivariable model</th>
<th>Unadjusted odds ratio†</th>
<th>95% confidence interval</th>
<th>Adjusted odds ratio‡</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TMP-SMX‡-resistant Enterobacteriaceae</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TMP-SMX at the facility level</td>
<td>1.14</td>
<td>1.06, 1.22</td>
<td>1.14</td>
<td>1.06, 1.22</td>
<td></td>
</tr>
<tr>
<td>Use of intravenous therapy in the nursing home</td>
<td>2.83</td>
<td>1.05, 5.0</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>No. of hand-washing sinks per 100 residents</td>
<td>3.5</td>
<td>1.1, 13.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of occupied beds per 100 residents</td>
<td>0.94</td>
<td>0.90, 0.98</td>
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<td></td>
<td></td>
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<tr>
<td><strong>MRSA‡</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Penicillins</td>
<td>0.90</td>
<td>0.80, 1.02</td>
<td>0.97</td>
<td>0.85, 1.10</td>
<td></td>
</tr>
<tr>
<td>Use of antimicrobial soap in the nursing home</td>
<td>0.40</td>
<td>0.18, 0.90</td>
<td></td>
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</tr>
<tr>
<td>Use of different soaps by staff and residents§</td>
<td>0.24</td>
<td>0.12, 0.47</td>
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<tr>
<td>Use of intravenous therapy in the nursing home</td>
<td>8.55</td>
<td>3.65, 20.0</td>
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<tr>
<td>No. of registered nurses per 100 residents</td>
<td>0.79</td>
<td>0.72, 0.87</td>
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<tr>
<td><strong>MRSA</strong></td>
<td></td>
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<tr>
<td>Fluoroquinolones</td>
<td>1.00</td>
<td>0.97, 1.03</td>
<td>1.00</td>
<td>0.97, 1.03</td>
<td></td>
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<tr>
<td><strong>Fluoroquinolone-resistant Enterobacteriaceae</strong></td>
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<tr>
<td>Fluoroquinolones</td>
<td>1.08</td>
<td>1.04, 1.11</td>
<td>1.08</td>
<td>1.04, 1.11</td>
<td></td>
</tr>
<tr>
<td><strong>Fluoroquinolone-resistant <em>Pseudomonas aeruginosa</em></strong></td>
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<td></td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>1.04</td>
<td>1.01, 1.07</td>
<td>1.04</td>
<td>1.01, 1.07</td>
<td></td>
</tr>
</tbody>
</table>

* Unadjusted odds ratios for antimicrobial exposures and adjusted odds ratios for variables kept in the final multivariable models are shown.
† Odds ratio for antimicrobial exposure per one defined daily dose per 100 resident-days.
‡ TMP-SMX, trimethoprim-sulfamethoxazole; MRSA, methicillin-resistant *Staphylococcus aureus*.
§ Use of antibacterial soap by staff and use of regular soap by residents.

percentages ranging from 0 to 100 percent (median of 29 percent in homes where it was detected). Twelve percent of *P. aeruginosa* were resistant to gentamicin. Thirty-three percent of *S. aureus* were methicillin-resistant, with the percentage ranging from 0 to 100 percent (median of 53 percent in homes where it was detected). There were no significant differences in the proportions of antibiotic-resistant bacteria between US and Canadian nursing homes.

### Antibiotic exposure and antibiotic resistance

The relations between various combinations of antibiotic exposure and antibiotic resistance are shown in table 3. All effects of antibiotic exposure are given in terms of odds ratios per defined daily dose per 100 resident-days. Receipt of TMP/SMX was a significant risk factor for TMP/SMX-resistant Enterobacteriaceae in nursing home residents (adjusted odds ratio (OR) = 1.14, 95 percent confidence interval (CI): 1.06, 1.22). Similarly, exposure to fluoroquinolones was a significant risk factor for fluoroquinolone-resistant Enterobacteriaceae (adjusted OR = 1.08 (95 percent CI: 1.04, 1.11) per defined daily dose per 100 resident-days) and fluoroquinolone-resistant *P. aeruginosa* (adjusted OR = 1.04 (95 percent CI: 1.01, 1.07) per defined daily dose per 100 resident-days). However, increased exposure to fluoroquinolones was not a risk factor for MRSA (adjusted OR = 1.00, 95 percent CI: 0.97, 1.03), nor was exposure to penicillins (adjusted OR = 0.97, 95 percent CI: 0.85, 1.10). Since none of the individuals with aminoglycoside-resistant bacteria were exposed to aminoglycosides, estimates of association at the individual level could not be determined.

### Infection control and other nursing-home-level factors

A number of factors relating to staffing and hand-washing were associated with antibiotic resistance. An increased number of registered nurses per 100 residents was associated with reduced MRSA in the model assessing penicillin exposure (adjusted OR = 0.79, 95 percent CI: 0.72, 0.87) (table 3). Use of antibacterial soap in the nursing home was associated with a reduced prevalence of MRSA (adjusted OR = 0.40, 95 percent CI: 0.18, 0.90). Similarly, use of different soaps by staff and residents (i.e., the staff used antibacterial soap while the residents used regular soap) was significant (adjusted OR = 0.24, 95 percent CI: 0.12, 0.47) when MRSA was modeled on penicillin use and also when MRSA was modeled on nursing home fluoroquinolone exposure (adjusted OR = 0.22, 95 percent CI: 0.13, 0.36). An increase in the number of hand-washing sinks per 100 residents was shown to reduce the risk of TMP/SMX-resistant Enterobacteriaceae (adjusted OR = 0.94, 95 percent CI: 0.90, 0.98).

Other factors at the level of the nursing home were associated with resistance to antimicrobial agents. An increase in the number of occupied beds in the nursing home significantly increased the risk of TMP/SMX-resistant Enterobacteriaceae (adjusted OR = 1.02, 95 percent CI: 1.00, 1.03). Use of intravenous therapy in the nursing home was strongly associated with MRSA in the penicillin model (adjusted OR = 8.55, 95 percent CI: 3.65, 20.0).

### DISCUSSION

We found that increased levels of nursing staff as well as use of antimicrobial soap protected residents of nursing...
homes against the acquisition of MRSA. Greater numbers of hand-washing sinks were protective against infection with TMP/SMX-resistant Enterobacteriaceae.

Little is known about the effect of staffing on antibiotic resistance in long-term care facilities. The association demonstrated in this study between increased staffing levels and reduced rates of MRSA is important, particularly given recent reductions in staffing in long-term care facilities (29). To our knowledge, this is the first report to demonstrate such a relation in long-term care facilities. Evidence exists that even under usual conditions, infection control practices in long-term care facilities are far from ideal. For example, in one nursing home study, gloves were changed appropriately in only 16 percent of direct care provisions between residents (30). In a study conducted by Pittet et al. (31) in a teaching hospital, nonadherence to hand-washing was greatest when the intensity of patient care was high. Better adherence to hand hygiene with increased staffing might therefore be the explanation for our findings. This is also supported by our finding that greater numbers of hand-washing sinks were protective against TMP/SMX-resistant Enterobacteriaceae. These findings are consistent with those of Kaplan et al. (32), who noted an increase in compliance with hand-washing with an increased ratio of sinks to beds in an intensive care unit. Our findings suggest that adequate staffing of nursing homes along with greater emphasis on hand hygiene may be important in limiting the spread of resistance to antimicrobial agents in nursing homes.

Use of antibacterial soap in the nursing home was associated with a reduced risk of MRSA among nursing home residents. Triclosan, the active ingredient in many antibacterial soaps, can effectively inhibit MRSA (33). This agent has been used to help interrupt outbreaks of MRSA in neonatal units (34, 35). There is little epidemiologic evidence to support or refute use of these agents in health care facilities. Our findings support the use of antibacterial soaps in the long-term care setting. A difference in the use of antibacterial soap between staff and residents—that is, the staff used antibacterial soap and the residents used regular soap—was also independently associated with a reduction in MRSA. These findings provide evidence to support the use of antibacterial soap among staff members in long-term care facilities. However, a definitive answer to the question of whether to use antibacterial soap in long-term care settings would be best derived from a randomized controlled trial.

TMP/SMX and fluoroquinolones, which accounted for over one third of all antibiotics prescribed in this study, were found to be independent risk factors for TMP/SMX and fluoroquinolone resistance in Enterobacteriaceae and P. aeruginosa, respectively. These findings are important, since Enterobacteriaceae cause the vast majority of urinary tract infections in residents of long-term care facilities, for which TMP/SMX is recommended as the antibiotic of choice (2). The association between fluoroquinolone exposure and Enterobacteriaceae or P. aeruginosa in nursing homes is consistent with previous reports from long-term care facilities (16, 36). Reducing inappropriate prescribing of these and other antimicrobial agents in the long-term care setting, such as for asymptomatic bacteriuria (37), may reduce the spread of antibiotic resistance in nursing homes.

The association between intravenous therapy and antibiotic-resistant bacteria (MRSA and TMP/SMX-resistant Enterobacteriaceae) was unexpected. For MRSA, this association may have been confounded by the use of vancomycin, which is used intravenously to treat MRSA infection. Individuals with MRSA infection may have been preferentially transferred from hospitals to nursing homes that administered intravenous therapy. This may have led to the spread of MRSA among residents in these homes, resulting in increased MRSA infection. Another possibility, one which relates to either MRSA or TMP/SMX-resistant Enterobacteriaceae, is that residents in nursing homes which used intravenous therapy were more debilitated and more susceptible to acquiring infection with MRSA or TMP/SMX-resistant Enterobacteriaceae.

Our findings provide evidence for the importance of infection control factors as well as antimicrobial exposure in the spread of antibiotic-resistant bacteria in nursing homes. Strengths of this study include the large number of nursing home residents and the measurement of antibiotic exposure and resistance at the individual level, inclusion of factors related to staffing and hand hygiene, and the assessment of risk factors for a number of types of bacterial resistance.

Because this study was conducted in nursing homes with 100 or more beds, the results may not be generalizable to smaller facilities. Although participating homes were significantly larger than nonparticipating homes, the average bed size (186 beds) was within the range (50–199 beds) of 80 percent of nursing homes in the United States (38). Fifty percent of nursing homes in the United States have 100 or more beds. The average length of stay of residents in our study was similar to the US national average (2.5 years vs. 2.4 years). The ratio of registered nursing staff to beds among the nursing homes in our study was the same as the national average (8.8 per 100 residents) (37).

We acknowledge that the lack of covariates at the individual level (such as underlying illnesses, decubitus ulcers, urinary catheters, feeding tubes) may have led to biased estimates of the effect of antibiotic exposure on antibiotic resistance at the individual level (23–25). Other exposures, such as previous hospitalization or prior receipt of antibiotics while in the hospital, may have influenced isolation of antimicrobial-resistant bacteria. Given the large number of nursing home residents in our study, obtaining data on individual-level covariates was not feasible. However, the relation between antimicrobial exposure and bacterial resistance was adjusted for nursing-home-level variables, including feeding tubes, urinary catheters, and use of intravenous therapy. Furthermore, rates of admission from acute-care hospitals as well as readmissions from hospitals were considered. Since treatment with active antibiotics may inhibit the growth of susceptible organisms, residents selected on the basis of having susceptible bacteria cultured may have been less likely to receive antibiotics than our source population of nursing home residents (39). Since obtaining all of the clinical isolates was beyond the scope of this study, molecular typing to establish the clonality of antimicrobial-resistant bacteria was not done.

In conclusion, we found in this study that increased staffing levels, use of antimicrobial soap, and an increase in
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