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## Antimicrobial Stewardship in Long-Term Care Facilities: A Call to Action

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### Abstract

Antimicrobial resistance is a global public health crisis and a national security threat to the United States, as stated in an executive order signed by the president in September 2014. This crisis is a result of indiscriminant antimicrobial use, which promotes selection for resistant organisms, increases the risk of adverse drug events, and renders patients vulnerable to drug-resistant infections. Antimicrobial stewardship is a key measure to combat antimicrobial resistance and specifically seeks to do this by improving antimicrobial use. Antimicrobial stewardship compliments infection control practices and it is important to note that these 2 disciplines are distinct and cannot be discussed interchangeably. Antimicrobial stewardship promotes the appropriate diagnosis, drug, dose, and duration of treatment. The appropriate diagnosis falls into the hands of the prescriber and clinical staff. Optimal antimicrobial drug selection, dosing strategy, and duration of treatment, however, often require expertise in antimicrobial therapy, such as an infectious disease-trained physician or pharmacist. Therefore, successful antimicrobial stewardship programs must be comprehensive and interdisciplinary. Most antimicrobial stewardship programs focus on hospitals; yet, in long-term care, up to 75% of antimicrobial use is inappropriate or unnecessary. Thus, one of the most pressing areas in need for antimicrobial stewardship is in long-term care facilities. Unfortunately, there is little evidence that describes effective antimicrobial stewardship interventions in this setting. This review discusses the need for and barriers to antimicrobial stewardship in long-term care facilities. Additionally, this review

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describes prior interventions that have been implemented and tested to improve antimicrobial use in long-term care facilities.

### Keywords

Antimicrobial stewardship program; antimicrobial resistance; long-term care; nursing home; antibiotic use

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Antimicrobial resistance is one of the greatest public health threats in the United States, prompting the president of the United States, the Centers for Disease Control and Prevention (CDC), and the World Health Organization to spearhead initiatives seeking effective solutions.<sup>1-3</sup> The prevalence of antimicrobial-resistant organisms is increasing throughout the United States, as is the use of “last line” and toxic antibiotics to treat infections caused by resistant bacteria.<sup>4</sup> The driving force that selects for antimicrobial-resistant bacteria and promotes *Clostridium difficile* infection is antimicrobial use.<sup>1</sup> Approximately 50% of antimicrobial use in hospitals and up to 75% of antibiotic use in long-term care facilities may be inappropriate or unnecessary.<sup>5,6</sup> As such, it is critically important to the safety of patients that antimicrobial use is improved throughout the entire health care system. Antimicrobial stewardship is typically defined as any activity to improve the drug, dose, duration, or route of an antimicrobial.<sup>7</sup> However, stewardship should also focus on an appropriate diagnosis. The primary goal of antibiotic stewardship is to optimize clinical outcomes while minimizing unintended consequences of antimicrobial use.

Implementation of new antimicrobial stewardship programs is challenging, requiring increased resources and time. Despite this, implementation of antimicrobial stewardship programs has been recommended for all health care settings in the United States, including long-term care facilities.<sup>7,8</sup> According to the CDC, over the next 5 years, approximately 619,000 infections due to resistant pathogens and *C difficile* could be prevented with the immediate and national implementation of antibiotic stewardship and infection control interventions.<sup>9</sup> In acute care facilities, comprehensive antimicrobial stewardship programs have been shown to improve the quality of patient care and safety. Through reduction of inappropriate antibiotic use and optimization of antimicrobial therapy, antimicrobial stewardship programs can reduce rates of *C difficile* infection and slow the emergence of antimicrobial resistance.<sup>10-12</sup> However, applying the evidence-based principles of antimicrobial stewardship developed in acute care facilities to long-term care facilities presents significant challenges.<sup>7</sup>

In an effort to support improved antimicrobial use, the Obama administration recently released an executive order (September 2014) and a National Action Plan (March 2015) for combating antibiotic-resistant bacteria.<sup>3,13</sup> This plan specifically calls for strengthening antibiotic stewardship in long-term care settings “by expanding existing programs, developing new ones, and monitoring progress and efficacy.”<sup>3</sup> Additionally, for the first time since 1991, the Centers for Medicare and Medicaid service (CMS) has now opened for comments their new proposed rules for long-term care facilities. Proposed recommendations include (1) a required infection prevention and control officer, and (2) an antibiotic stewardship program that includes antibiotic use protocols and a system to monitor antibiotic

use. Additionally, the CDC recently released 7 Core Elements of antimicrobial stewardship in long-term care facilities, including (1) facility leadership commitment, (2) accountability, (3) drug expertise, (4) actions to improve use, (5) education, (6) tracking, and (7) reporting.<sup>14</sup> Although progressive, these recommendations face many challenges, particularly due to the paucity of evidence on effective antimicrobial stewardship practices in long-term care. Here, to help advance these efforts, we review the literature describing antimicrobial stewardship efforts in long-term care. Specifically, we discuss the need for and barriers to antimicrobial stewardship in long-term care facilities as well as previous strategies that have been implemented to improve antimicrobial use in this unique setting.

## Methods

We conducted a structured review of existing literature related to antimicrobial stewardship in long-term care facilities. This review was conducted to identify (1) the need for antimicrobial stewardship in long-term care facilities, (2) barriers to antimicrobial stewardship in long-term care facilities, and (3) previous studies related to implementation of antimicrobial stewardship interventions in long-term care facilities. We used Medline to perform the structured search using the following relevant key words: antimicrobial stewardship, antimicrobial use, long-term care facility, and nursing home. References in English dated between 1966 and June 2015 were considered. We also conducted a follow-up Internet Search and search of reference lists from relevant studies. Based on a review of titles and abstracts, documents were selected for full text review if they fell into 1 of the 3 categories. All documents selected for full-text review were included in our review article. To describe and synthesize intervention literature, the following were collected from each article: year of publication, infection type, study design, study setting, intervention, unit of analysis, and major findings.

## Results

We selected 67 articles for inclusion based on full-text review. Of these, 30 (44.8%) articles were categorized as needs for antimicrobial stewardship, 26 (38.8%) as barriers to antimicrobial stewardship, and 15 (22.4%) as prior studies related to implementation of antimicrobial stewardship interventions in long-term care facilities. Four (6.0%) articles addressed more than 1 category. Needs for antimicrobial stewardship in long-term care can be found in Table 1. These articles included 23 (76.7%) observational studies, 5 (16.7%) review articles, and 2 (6.7%) professional society guidelines. Barriers to antimicrobial stewardship in long-term care can be found in Table 2. These articles included 9 (34.6%) review articles, 5 (19.2%) professional society guidelines/recommendations, and 4 (15.4%) observational studies.

Prior studies related to implementation of antimicrobial stewardship interventions in long-term care facilities can be found in Tables 3 and 4. These articles included 8 (53.3%) quasi-experimental studies, 5 (33.3%) randomized controlled trials, 1 (6.7%) pre- versus post-intervention survey, and 1 (6.7%) systematic review. Of the articles that tested an intervention (n = 14), 78.6% were multifaceted educational interventions. Studies that

assessed the impact of interventions on general antibiotic use were most common (n = 7, 50.0%), followed by interventions that target a specific syndrome (n = 7, 50.0%).

## Discussion

### Need for Antimicrobial Stewardship in Long-Term Care Facilities

In 2013, approximately 1.4 million adults received nursing home care at one of the more than 15,700 facilities in the United States.<sup>15</sup> As a group, the residents of long-term care facilities represent some of the oldest and frailest members in our communities.<sup>16</sup> Based on results from the 2004 National Nursing Home Survey, 45% of nursing home residents were aged 85 years and older, with an average length of stay of 2.3 years.<sup>17</sup> Nearly 80% were dependent for assistance with at least 4 of the 5 activities of daily living: toileting, bathing, transfer, dressing, and eating. Increasing age, frailty, immune senescence, and comorbid conditions render long-term care facility residents vulnerable to infection. Even for experienced clinicians, determining whether a long-term care resident has an infection presents significant challenges. This may contribute to the high prevalence of antibiotic use in this population.<sup>18,19</sup>

### Inappropriate and Unnecessary Antibiotic Use in Long-Term Care Facilities

Antimicrobials account for almost half of all prescriptions in long-term care facilities.<sup>20,21</sup> It is estimated that 50% to 75% of residents receive at least one course of an antibiotic each year.<sup>22-24</sup> Unfortunately, many of these prescriptions represent overuse or inappropriate use.<sup>25</sup> A study of 2 community-based nursing homes in Rhode Island found several types of inappropriate antibiotic prescribing patterns related to urinalyses ordered on 172 case residents. Antibiotic treatment was initiated in 70 case residents (41%) that did not meet the McGeer criteria. Additionally, 72% of case residents received an inappropriate drug based on Infectious Diseases Society of America criteria, 46% were dosed inappropriately based on creatinine clearance, and 67% received treatment for longer than recommended.<sup>26</sup> A study that reviewed antimicrobial orders from 42 skilled nursing facilities found that 38% of orders were inappropriate.<sup>27</sup> Similarly, in a retrospective chart review of systemic antimicrobial regimens administered to residents of a 160-bed Veterans Affairs (VA) skilled nursing facility, 43% of the 1351 days of antimicrobial therapy were deemed unnecessary and 49% of residents received at least 1 day of unnecessary antimicrobial therapy.<sup>6</sup> The most common reasons for entirely and partially unnecessary regimens were asymptomatic bacteriuria and longer than recommended treatment durations, respectively.

Inappropriate antibiotic prescriptions not only originate in the long-term care facility, but also in other settings in which residents receive care. For example, a resident may be sent to the emergency department for a potentially noninfectious cause, such as delirium or agitation, and be sent back to the nursing home with an inappropriate antimicrobial prescription. Additionally, a resident may be discharged from the hospital with an antimicrobial prescription that was not indicated, was the wrong drug or dose, or was continued for too long a duration.<sup>26</sup> A resident also may be prescribed an inappropriate antibiotic at a specialist visit, such as urology, rheumatology, dermatology, or even through

an infectious diseases (ID) consult, all of which may contribute to the high prevalence of inappropriate use among long-term care facilities.

### Increased Risk for Colonization With Resistant Bacteria

On average, at least 30% to 50% of long-term care residents are colonized with 1 or more resistant organisms, and colonization can lead to subsequent infection, particularly in older, frail residents.<sup>28–34</sup> The primary mode of introduction of resistant organisms into this setting is the transfer of infected or colonized residents from acute care hospitals to long-term care facilities.<sup>35</sup> Acute care facilities and long-term care facilities are connected through shared residents. A recent study using the Long-Term Care Minimum Data Set revealed a high volume of bidirectional flow between long-term care facilities and acute care hospitals.<sup>36</sup> During the 15-month study period, there were more than 2 million discharges from long-term care facilities to acute care hospitals and more than 4 million admissions to long-term care facilities from acute care hospitals.<sup>36</sup> As an example, long-term care residents in a regional health system in Iowa colonized with vancomycin-resistant enterococci were significantly more likely than noncolonized residents to have been hospitalized at an acute care facility (19/30 vs 12/66; odds ratio [OR] 8.0; 95% confidence interval [CI] 2.7–23.8).<sup>37</sup> However, long-term care facilities residents may be seen as reservoirs of resistant bacteria, and also can transport resistant organisms to the acute care setting or into the community.<sup>35,38</sup>

Methicillin-resistant *Staphylococcus aureus* (MRSA) colonization among long-term care residents can be as high as 60%, as identified in one study among 412 residents at 3 separate long-term care facilities.<sup>31</sup> A point-prevalence survey of long and short-term acute care facilities in Chicago found the prevalence of those colonized with carbapenem-resistant Enterobacteriaceae was much higher among residents in long-term care facilities compared with patients in acute care facilities (30.4% vs 3.3%).<sup>39</sup> Factors that increase the risk of colonization with multidrug-resistant organisms relate both to residents health and their environment. Exposure to multiple courses of antibiotics select for resistant bacteria. Other factors that increase the risk of colonization by resistant bacteria for long-term care facility residents include poor nutritional status, skin and soft tissue breakdown, and the presence of multiple devices, including gastrostomy tubes and/or indwelling catheters.<sup>35</sup> In an effort to support a homelike environment, long-term care facilities encourage social interaction in shared spaces. Unfortunately, these practices may increase opportunities for residents to disseminate and acquire resistant organisms through shared dining rooms, rehabilitation equipment, and recreation areas. Among long-term care residents, independent risk factors found to be associated with colonization for multidrug-resistant organisms include prior colonization or infection by multidrug-resistant organisms, hospitalization in the past 3 months, recurrent urinary tract infections, peripheral arterial disease, current wound management, medical devices in situ, pressure ulcers, advanced dementia, and prolonged antibiotic use.<sup>32,33</sup>

### Increased Risk of *C difficile* Infections

*C difficile* infections are another major concern in the long-term care environment.<sup>40</sup> *C difficile* infections are endemic in many facilities, despite efforts to manage the burden of *C*

*difficile* infections in this setting.<sup>41</sup> Up to 30% of residents treated with antibiotics in long-term care facilities acquire *C difficile*.<sup>42</sup> Residents in 2 Rhode Island nursing homes who received inappropriate antimicrobials for asymptomatic bacteriuria were 8.5 times more likely to develop *C difficile* infections compared with the rest of the nursing home population (95% CI 1.7–42.0).<sup>26</sup> Although exposure to systemic antibiotics and to *C difficile* spores often occurs in acute care hospitals, symptom onset may not develop until after the resident is transferred to the nursing home.<sup>43</sup> Importantly, older residents who develop *C difficile* infections are more likely to develop severe complications.<sup>44,45</sup>

Older adults, including long-term care residents, are also at increased risk for recurrent disease.<sup>46</sup> In 2006, the Ohio Department of Public Health mandated reporting of health care–onset *C difficile* infection, using standardized case definitions.<sup>46</sup> Although the incidence rate of first-time *C difficile* infection in 2006 was lower in long-term care facilities than hospitals (up to 2.9 vs 7.9 cases per 10,000 patient days), the absolute number of *C difficile* infections was higher in long-term care facilities (11,200 vs 7000 cases). For recurrent cases, the mean number of cases per month was higher in long-term care facilities (358 vs 108).<sup>46</sup> The incidence of recurrent cases for long-term care facilities and hospitals was as high as 2.4 cases and 2.0 cases per 10,000 patient-days, respectively, for the reporting period.

### Barriers to Antimicrobial Stewardship in Long-Term Care Facilities

The prevalence of antimicrobial stewardship (various definitions used) among long-term care facilities varied greatly in 3 large statewide/regional surveys from approximately 25% to 60%.<sup>47–49</sup> In our literature review, we identified several barriers to formalizing antimicrobial stewardship programs in long-term care (Table 2). These barriers are notable and can impede the implementation and success of these programs. One of the main challenges includes a paucity of well-validated strategies specific to long-term care facilities, as evidenced by limited finding of studies to improve antimicrobial use in long-term care facilities (Tables 3 and 4).

In general, in long-term care facilities, a clinical event suggestive of infection, such as a fever, prompts an evaluation of the affected resident followed by an antimicrobial prescription. Unfortunately, few people who work at nursing homes possess specialized knowledge or access to educational resources on antimicrobial use and infection management.<sup>50–54</sup> Nurses usually conduct the initial evaluations of residents.<sup>50</sup> In many facilities, nurses are the only licensed health care professionals available on-site 24 hours a day.<sup>55</sup> Fewer than 20% of nursing homes employ full-time staff physicians.<sup>56</sup> Providers are most often off-site, splitting their time between other long-term care facilities and office-based practice. A survey of medical directors found that they provide primary care at an average of 4 facilities, where they spend 8 to 12 hours a week providing care to residents, while also serving as a medical director to 2 facilities.<sup>56</sup> Therefore, providers must rely on nursing staff to assess changes in a resident's status and then communicate their findings via phone or fax.<sup>18</sup> The timing and quality of these communications, as well as professional practice patterns, often favor antimicrobial prescriptions as the “safest,” and often most expedient, course of action. Physicians at one hospital reported that they often prescribe

treatment for urinary tract infections without seeing the residents and rely on nurses to provide information regarding the signs and symptoms of urinary tract infection.<sup>57</sup> Another study found that only 44% of residents who received antibiotics had an associated claim for a bedside visit by a physician within 1 day of their prescription.<sup>58</sup>

### Resource Limitations

Additional barriers include lack of funding and facility resources.<sup>7,19,48</sup> For example, tools to measure antibiotic use or to develop antibiograms in long-term care have thus far been limited. Another barrier is that many long-term care facilities do not have onsite microbiology laboratories, which may delay reporting of organism identification and susceptibility results, and any resultant stewardship interventions.<sup>59</sup> Additionally, few facilities have on-site chemistry laboratories or radiologic equipment, thus hindering ready access to many diagnostic tests, such as complete blood counts or chest films. The delays inherent to arranging for these tests may significantly delay the clinician's ability to make a prompt and accurate diagnosis.

### Need for Diagnostic Criteria and Treatment Pathways: Focus on Urinary Tract Infections

The proper diagnosis and treatment of infection in residents is itself a barrier to antimicrobial stewardship. Diagnosing infections in older residents can be exceedingly challenging due to many factors, such as comorbid disease states, blunted immune response, vague symptoms, cognitive impairment, and high rates of colonization with drug-resistant bacteria.<sup>50</sup> Suspected urinary tract infections (UTIs) in this population are particularly challenging.

In long-term care settings, the most common reason residents receive antimicrobials is concern for a UTI.<sup>60–63</sup> Diagnostic criteria for UTIs include acute dysuria, fever, leukocytosis, and symptoms that localize to the urinary tract along with bacterial growth from an appropriately collected urine sample.<sup>64</sup> Distinct from UTI is *asymptomatic bacteriuria*, in which older adults have positive urinalyses and urine cultures without any systemic signs or symptoms of illness (also referred to as “dirty urine”).<sup>65</sup> The prevalence of asymptomatic bacteriuria is high in this population, affecting 15% of community-dwelling older adults and 50% of long-term care facility residents.<sup>65</sup> Some health care providers respond to any positive urine culture from an older adult by prescribing antimicrobials, regardless of whether symptoms of a UTI are present, even though treatment has not been shown to decrease the incidence of symptomatic UTIs, nor has it been associated with a decrease in morbidity or mortality.<sup>65</sup> This is concerning because there is a strong association between the treatment of asymptomatic bacteriuria and the subsequent emergence of resistant organisms.<sup>66,67</sup>

Treatment of asymptomatic bacteriuria is especially problematic in residents with indwelling urinary catheters. In a cross-sectional study of antibiotic prescription data for residents from 4 nursing homes in Texas, the strongest predictor of antibiotic treatment for asymptomatic bacteriuria was the presence of an indwelling urinary catheter.<sup>68</sup> For residents with urinary catheters, more than 80% of the antibiotics prescribed were for asymptomatic bacteriuria. In residents without a catheter, approximately 50% of prescriptions were for residents with no

documented UTI symptoms. Alarming, multivariate analyses demonstrated that resident characteristics did not affect whether an antibiotic was prescribed for asymptomatic bacteriuria. Moreover, the only significant factor identified was the nursing home itself. This evidence suggests that the practices of providers may drive treatment for suspected UTIs, rather than the clinical characteristics and symptoms of the resident. Thus, efforts to improve prescriber practices with regard to the treatment of suspected UTIs may be an important focus of antimicrobial stewardship interventions in long-term care facilities.

### **Lack of Trained ID Physicians and Pharmacists**

Formal training in ID and/or antibiotic stewardship is recommended for antimicrobial stewardship program leaders.<sup>7,69</sup> However, few formal residency and fellowship programs provide specialized training in antimicrobial stewardship for physicians and pharmacists.<sup>53,54</sup> A recent survey of long-term care facilities in Rhode Island demonstrated that approximately 80% of facilities did not have any full-time equivalent ID physicians or pharmacists facility-wide.<sup>49</sup>

### **Resident and Family Expectations**

Efforts to promote the judicious use of antibiotics in long-term care also may be hampered by expectations from residents and family members. In a recent prospective cohort study, in 35 Boston-area nursing homes on health care proxy involvement in decisions on residents with advanced dementia, involvement was associated with both increased antibiotic use (adjusted OR 3.43, 95% CI 1.94–6.05) and hospital transfer (adjusted OR 3.00, 95% CI 1.19–7.53).<sup>70</sup> This trend is likely influenced by a general fear of litigation on the part of the provider. Studies suggest that long-term care physicians often operate in a state of high legal anxiety that may prompt more aggressive care and unnecessary transfers out of the nursing home.<sup>71</sup> When notified about a complex medical resident with nonspecific symptoms, nursing home providers often err on the side of caution.<sup>72</sup>

### **What Works to Improve Appropriate Antimicrobial Use in Long-Term Care Facilities?**

Few randomized controlled trials have evaluated interventions to reduce inappropriate antimicrobial use in long-term care facilities (Table 3). A recent systematic review identified only 4 randomized controlled trials designed to reduce inappropriate antimicrobial use in this setting.<sup>73</sup> All of these studies provided educational material to physicians and nurses<sup>74–76</sup> or to physicians only,<sup>77</sup> with 2 studies also incorporating prescribing feedback.<sup>76,77</sup> As Table 3 shows, all 4 studies produced either a decrease in antibiotic use or an increase in the prevalence of appropriate antibiotic use.<sup>74–77</sup> However, overall, the quality of evidence was weak, the results were mixed, and the interventions implemented varied greatly. Nonetheless, these findings support multifaceted interventions, which include educational strategies, as well as locally developed guidelines, and prescribing feedback to improve antimicrobial prescribing in the long-term care setting.<sup>73</sup> However, there has been no standardization of programs, and multiple components designed to improve antimicrobial use are often implemented simultaneously, so the efficacy or effectiveness of any one program component is largely unknown.<sup>19</sup>



## Multifaceted Educational Interventions Targeting General Antibiotic Use for All Infection Types

Antimicrobial stewardship programs that use multiple educational modalities have generally been effective at improving antimicrobial use for the treatment of both infections in general and specific infection types (discussed later in this article).<sup>57,78–81</sup> The types of educational interventions and the combinations of stewardship interventions assessed to date have varied greatly in the literature (Table 4). Examples of strategies studied include educational sessions, academic detailing, prescribing feedback, and/or dissemination of written materials, such as guidelines, algorithms, pocket cards, posters, and toolkits.

Multifaceted educational intervention studies that target only providers have yielded modest results (Table 4).<sup>77,81</sup> The impact of an educational intervention for physicians was assessed in a cluster randomized controlled trial among long-term care facilities in Montreal, Canada.<sup>77</sup> In intervention facilities, physicians were mailed an antibiotic guide and feedback on their prescribing practices over the previous 3 months. This intervention was then repeated 4 months later. By the end of the study, there was a greater decrease in antibiotic orders, which did not adhere with the guide in the intervention homes versus control (usual care) homes (–20.5% vs –5.1%). After the second mailing, physicians were 64% less likely to prescribe nonadherent antibiotics (OR 0.36, 95% CI 0.18–0.73), but this effect was not sustained 15 months later (OR 0.48, 95% CI 0.23–1.02). Similarly, an uncontrolled single-center quasi-experimental study at a public hospital with 340 long-term care beds assessed the impact of educational sessions with feedback and guidelines on antibiotic use for physicians.<sup>81</sup> Postintervention, 39% of antibiotic use was compliant with guidelines as compared with 11% preintervention ( $P < .001$ ). During the intervention, antimicrobial use and antimicrobial starts decreased 29.7% and 25.9%, respectively. Notably, an interrupted time-series analysis indicated that the overall decrease in antimicrobial use persisted for 2 years following the intervention period. The availability of ID consultations at this long-term care facility may have contributed to the longevity of the success of this intervention.

Due to the significant role nurses play in recognizing, assessing, and monitoring residents with infections, nurses may be an important target for educational interventions aimed at improving antimicrobial use in long-term care facilities. The impact of a multifaceted educational intervention for nurses and physicians was tested in a cluster randomized controlled trial among 58 nursing homes in Sweden.<sup>76</sup> The main components of the intervention included small group educational sessions for nurses and physicians, feedback on prescribing, presentation of guidelines, and written materials. Although there was no significant impact on the primary outcome, proportion of quinolones prescribed for lower UTI, the intervention did achieve a significant reduction in the proportion of infections treated with antibiotics (absolute risk reduction [ARR] –0.124, 95% CI –0.228 to –0.019) and a significant increase in the proportion of infections handled by physicians as “wait and see” (ARR 0.143, 95% CI 0.047–0.240). Similarly, a quality improvement program that included educational sessions to providers and nurses; a medical care referral form; prescriber feedback; and education for staff, residents, and families was associated with a significant reduction in antibiotic prescribing rates for all indications assessed.<sup>80</sup>

## Educational and Academic Detailing Interventions Targeting Pneumonia

Multifaceted educational interventions targeting pneumonia have had only a limited impact on improving antibiotic use (Table 4). Three studies have assessed the impact of implementing nursing home-acquired pneumonia (NHAP) guidelines through educational programs.<sup>75,82,83</sup> Two of these studies, which both assessed the impact of educational sessions for nurses and academic detailing to physicians failed to demonstrate improvement in antimicrobial use.<sup>82,83</sup> A controlled, quasi-experimental study in 2 state Veterans Homes found guideline adherence with respect to choice and timing of antibiotics did not improve significantly postintervention at the intervention facility.<sup>82</sup> However, this study did find guideline adherence for these measures was higher at the intervention facility as compared with the control facility, during the intervention period.

The second study used a controlled quasi-experimental design among 16 nursing homes in Colorado and Kansas to assess the impact of a multifaceted intervention to improve adherence to the NHAP guidelines.<sup>83</sup> The intervention included educational sessions for nurses to improve recognition of pneumonia symptoms and timing of antibiotics and academic detailing to prescribers by pharmacists regarding diagnostic and treatment practices over the influenza seasons (October to April) of 2005/2006 and 2006/2007. This study found no significant impact on guideline adherence for choice of antibiotic or duration; however, improvements in adherence to timely antibiotics were significantly higher in intervention homes compared with control homes. Neither study found improvements in clinical outcomes, such as mortality and hospitalization rates, postintervention. The impact of these interventions may have been higher if (1) education had also been provided to nurses, (2) academic detailing had been facilitated by a multidisciplinary team, (3) the intervention period had been longer in duration, or (4) education had been provided to residents and family members or caregivers.

The third study, a randomized controlled study among 10 skilled nursing facilities, assessed the impact of small-group education for providers only versus providers and nurses.<sup>75</sup> The proportion of antibiotic use meeting guidelines (pre: 50% vs post: 81.8%,  $P = .06$ ) improved with the multidisciplinary intervention that targeted both providers and nurses, whereas the physician-only intervention did not have a significant effect (pre: 64.5% vs post: 69%,  $P = .73$ ). However, in multivariate analysis, treatment according to the guidelines was not significantly different between the multidisciplinary and physician-only intervention groups. This study similarly found no significant differences in overall antibiotic use, mortality, or hospitalization rates.

## Education to Prevent Misdiagnosis and Overtreatment of Presumed UTIs

Interventions to improve antimicrobial use for presumed UTIs have generally demonstrated greater success than those targeting pneumonia (Table 4). A cluster randomized controlled trial assessed the impact of a multifaceted intervention targeting suspected UTIs on intervention and control nursing homes in Ontario, Canada.<sup>74</sup> A diagnostic and treatment algorithm for UTIs was implemented by using multiple modalities, including small group educational sessions for nurses, videotapes, written materials, outreach visits, and interviews with physicians. This intervention was associated with significant improvements in

antimicrobial prescriptions for suspected UTIs (pre: 1.59 vs post: 1.17 courses per 1000 resident days; weighted mean difference  $-0.49$ , 95% CI  $-0.93$  to  $-0.06$ ) and a nonsignificant reduction in urine cultures obtained (pre: 2.48 vs post: 2.03 cultures per 1000 resident days; weighted mean difference  $-0.51$ , 95% CI  $-1.38$  to  $0.35$ ). Unfortunately, the effect on antimicrobial prescriptions was not sustained during a 12-month postintervention observation period. Additionally, the study did not report significant differences in mortality or hospital admissions.

An uncontrolled quasi-experimental study assessed the effect of a multifaceted educational intervention, which included individualized direct feedback for nurses and providers, to reduce inappropriate treatment of asymptomatic bacteriuria.<sup>57</sup> The rate of treatment of asymptomatic bacteriuria (pre: 1.7 to post: 0.6 asymptomatic bacteriuria treated per 1000 resident days; incidence rate ratio [IRR] 0.37, 95% CI 0.19–0.72,  $P = .002$ ) and inappropriate submission of urine cultures (pre: 2.6 to post: 0.9 cultures per 1000 resident days; IRR 0.36, 95% CI 0.21–0.62,  $P < .001$ ) decreased significantly 6 months postintervention and these reductions were sustained for 30 months.

A multidisciplinary team, including an ID consultant, an infection control nurse, and a geriatrician, provided academic detailing concerning the diagnosis and treatment of UTIs to head practitioners and head nurses at all long-term care facilities for older persons in Finland during 2004 to 2005.<sup>78</sup> After the visits, regional guidelines were developed and published and an annual questionnaire was mailed to the head nurse of each unit. This multifaceted intervention was associated with a significant reduction in the proportion of residents on antibiotic prophylaxis for urinary tract infections (14.5% in 2005 vs 7.8% in 2008,  $P < .001$ ). Most recently, a controlled, quasi-experimental study among 2 VA Healthcare System Medical Centers, both of which included long-term care and general medicine wards, found a multifaceted educational program, which included individualized feedback to clinicians, was associated with significant reductions in overtreatment of asymptomatic bacteriuria in intervention versus comparison sites (long-term care residents only; intervention period: 20% vs 40%, maintenance period: 10% vs 19.2%).<sup>79</sup>

### Antimicrobial Stewardship Tool

An antimicrobial stewardship tool for nurses in long-term care facilities was associated with significant decreases in total antibiotic use.<sup>55</sup> This tool to promote appropriate use of antibiotics was a preprinted form with 2 parts to be completed by nurses at treatment initiation and 48 to 72 hours after starting treatment. Other educational interventions implemented included a support pack, a dedicated telephone number for the project, follow-up visits, posters, and promotional material. The support pack included signs and symptoms of infections in elderly individuals, obtaining clinical cultures, and information on resistance. Postintervention there was a significant 4.9% decrease (95% CI 1.0%–8.6%,  $P = .02$ ) in total antibiotic consumption in the intervention group (3.25 less defined daily doses per 1000 resident days) and a 5.1% increase (95% CI 0.2%–10.2%,  $P = .04$ ) increase in the control group (2.42 more defined daily doses per 1000 resident days). Total antibiotic consumption for prophylaxis of infection, and appropriateness of prescribing (measured by proportion of residents who fully met McGeer Criteria and also by proportion of residents

who fully met the minimum Loeb Criteria) improved postintervention. Additionally, no adverse events related to the tool were identified.

### **ID Consult Services**

A recent quasi-experimental study assessed the impact of an ID consult service implemented as a 160-bed VA long-term care facility.<sup>84</sup> This consult service included an ID physician and nurse practitioner who provided on-site weekly rounds. The remainder of the week they were available for remote consultation. This service was associated with a reduction in total antimicrobial use by 30% ( $P < .001$ ), fluoroquinolones by 38% ( $P < .001$ ), and  $\beta$ -lactam/ $\beta$ -lactamase inhibitor combinations by 28% ( $P < .001$ ). Additionally, the rate of positive *C. difficile* tests declined significantly postintervention as compared with preintervention ( $P = .04$ ). Because this was a VA facility, these findings may be not easily translated to community-based facilities.

### **Antibiograms**

The utility of antibiograms in improving antimicrobial use in acute care facilities is well recognized; however, their use in long-term care facilities is relatively unknown. Antibiograms are cumulative summaries of antimicrobial susceptibilities of local bacterial isolates over a period of time, usually 6 months or a year.<sup>85</sup> Clinicians typically use antibiograms to assess local susceptibility rates, which aids in the selection of appropriate empiric antibiotic therapy. One study specifically evaluated the impact of an antibiogram in a community-based skilled nursing facility.<sup>86</sup> Appropriate antibiotic empiric prescribing, defined in this study as an antibiotic choice that sufficiently covered the infecting organism based on antibiotic susceptibilities (ie, facility-specific antibiogram), increased from 32% to 45% after implementing the facility-specific antibiogram ( $P = .32$ ).

### **Measuring Outcomes and Metrics in Long-Term Care**

Based on our experience with antimicrobial stewardship and our review of the literature, we have additional ideas on how to advance antimicrobial stewardship in long-term care, which will be discussed throughout the remainder of our article. The studies conducted to date have mostly focused on the impact of antimicrobial stewardship programs on antimicrobial utilization. Although this is often the easiest outcome to measure, overall antibiotic use alone is not the strongest surrogate endpoint for improving resident safety and clinical outcomes. Declines in antibiotic use may not capture appropriate use because appropriate use means not only nonprescribing when an indication is absent but also proper prescribing when indicated. Instead, change in use should be targeted based on areas of high resistance or overuse. Additionally, a standard definition of appropriate use is needed because it varies greatly in the literature.

More research is needed using metrics that capture hard endpoints of resident safety and clinical outcomes rather than surrogate measures; however, doing this type of research is challenging. The studies conducted to date provide the important foundation needed to begin to conduct this type of research in the future. At this time, none of the studies reviewed assessed the impact of their intervention on antimicrobial resistance or total costs of care. Few studies attempted to measure clinical outcomes, such as reductions in mortality or

adverse events, or health care utilization, such as reductions in rates of emergency department visits and hospitalizations, as a result of improvements in appropriate antibiotic use. Moreover, no single study was able to provide a comprehensive assessment of their intervention on all the important outcomes of such a program, including antimicrobial utilization, health care utilization, costs, resistance, and clinical outcomes, including relevant adverse outcomes such as *C difficile* infection and adverse drug events. Finally, assessing the sustainability of implemented strategies is a worthy future research endeavor.

### Future of Antimicrobial Stewardship in Long-Term Care

Continued research must be done to broaden the arsenal of stewardship interventions in long-term care and to identify the most effective strategies. Antimicrobial stewardship guidelines for the acute care setting recommend a multidisciplinary approach and support from hospital leadership.<sup>7</sup> These principles may also be important in the long-term care setting, but require further investigation. Due to important differences between acute care hospitals and long-term care facilities, the ability to obtain financial support from leadership for antimicrobial stewardship multidisciplinary personnel and other resources may be challenging. However, as the CDC has recently recommended, leadership should at least demonstrate their support for antimicrobial stewardship through written statements.<sup>14</sup> Leadership should sign and support a written antimicrobial stewardship policy that should be shared with staff, residents, and families. Additionally, leadership can include stewardship-related duties in position descriptions and create a culture that promotes antimicrobial stewardship.<sup>14</sup> Additionally, for now, there is a call for the infection prevention control officer to work together with a physician or pharmacist to champion antimicrobial stewardship needs.

Support and collaboration of administration and clinicians are essential to the success of any antimicrobial stewardship program.<sup>7</sup> This support can be obtained through effective and local champions or leaders.<sup>87</sup> Champions are individuals who take ownership over the mission of the program and advocate for and support antimicrobial stewardship interventions.<sup>87</sup> Champions can help empower both leadership and staff to support antimicrobial stewardship efforts. The CDC recently recommended that nursing homes identify individuals accountable for antimicrobial stewardship to empower and engage leadership and staff.<sup>14</sup> For facilities in which stewardship is one of several competing priorities, an administrative champion such as the medical director can argue the case for antimicrobial stewardship to other medical staff leadership. Peer clinical champion or champions are also critically important. Well-respected clinicians, such as physicians, pharmacists, or nurses, with training in antimicrobial stewardship are ideally suited to act as peer champions. Peer champions should be committed to spearheading the program, and educating and gaining acceptance of other clinicians and staff on the program. Without written policies, “championing” for antimicrobial stewardship action may be difficult, therefore the champion should consider developing policies that promote optimal antibiotic use.

Many long-term care facilities across the country use central fill pharmacies and automated medication and supply systems. A central fill pharmacy is one that processes and fills

prescriptions for several local long-term care facilities. Therefore, the central fill pharmacy and pharmacists at those sites can play a unique role in promoting appropriate antimicrobial use within the local long-term care facilities they serve. Pharmacists are ideally suited to ensure that for each antimicrobial order an infectious diagnosis is documented, and can make recommendations on appropriate drug choice, dose, and duration using a facility's local antibiogram and treatment pathways.<sup>69</sup> A clinically trained ID pharmacist's specialized knowledge of pathogenic microbiology, drug-resistance, pharmacotherapy, drug-drug interactions, pharmacokinetics (ie, absorption, metabolism, distribution, and excretion of antibiotics) and pharmacodynamics (ie, maximizing antimicrobial killing/activity profiles) allows them to meaningfully contribute to antimicrobial stewardship. They can provide educational "in-services," assist in treatment pathway development, and recommend alternative antimicrobial choices at time of prescribing. However, busy pharmacists at central fill locations may not have protected workload time for antimicrobial stewardship activities, and thus other daily responsibilities may take precedence over stewardship. Additionally, the central fill pharmacy may not have access to clinically trained ID pharmacists. Therefore, training staff through antimicrobial stewardship certification programs may be a helpful option. Fortunately, there are antimicrobial stewardship certificate training programs among other informal training opportunities available for interested pharmacists and providers.<sup>88,89</sup>

Other strategies to advance stewardship include bringing staff with antibiotic expertise to long-term care facilities. Several facilities could share an ID consultant or a facility could share an ID consultant with a local acute care hospital to mitigate the cost of obtaining these individuals. Federal agencies are likely to continue to increase antimicrobial stewardship demands on long-term care facilities to improve the safety of residents; however, resources are not likely to increase. As such, there is a critical need to develop minimally sufficient and direct antimicrobial-focused interventions, which can effect significant reductions in inappropriate antimicrobial use with the least amount of resources.

## Conclusion

Antimicrobial resistance is a global public health crisis, one that has been accelerated through indiscriminant antimicrobial use. Antimicrobial stewardship programs have been recommended across all facets of health care to improve antimicrobial use and combat antimicrobial resistance; however, in the long-term care setting, effective antimicrobial stewardship interventions are largely unknown. High prevalence of antimicrobial use and resistant bacteria, coupled with limited resources, plague effective antimicrobial stewardship in this setting. Our review identified only 14 studies of antimicrobial stewardship interventions in long-term care. Overall, the quality of evidence was weak, the results were mixed, and the interventions varied greatly, as did study definitions and outcomes measures, such as "appropriate use." Several studies suggest that multifaceted educational interventions may be effective in increasing appropriate antimicrobial use in long-term care facilities. However, there is a critical need for future well-designed studies to develop tailored interventions to improve the care of the 1.4 million residents of long-term care facilities across the United States.

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**Table 1**

Needs for Antimicrobial Stewardship in Long-Term Care Facilities

| <b>Needs Identified</b>   |
|---|
| High prevalence of inappropriate and unnecessary antibiotic use                       |
| Increased risk for colonization with resistant bacteria                               |
| Increased risk of <i>Clostridium difficile</i> infections and potential complications |

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**Table 2**

**Barriers to Antimicrobial Stewardship in Long-Term Care Facilities**

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| <b>Barriers Identified</b>  |
|---|
| Paucity of well-validated strategies specific to long-term care facilities                |
| Lack of funding and facility resources, such as lack of on-site microbiology laboratories |
| Challenges associated with proper diagnosis and treatment of infection in residents       |
| Lack of trained ID physicians and pharmacists   |
| Resident and family expectations  |

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**Table 3**  
Randomized Controlled Trials to Improve Antimicrobial Use in Long-Term Care Facilities

| Study: Primary Author and Year of Publication  | Infection of Interest  | Design  | Setting   | Intervention  | Unit of Analysis  | Main Outcomes/Results  |
|--|--|---|---|---|---|--|
| Naughton 2001<br><b>Overall findings:</b><br><i>Education targeting pneumonia did not significantly change antibiotic use (PO or IV) or resident outcomes.</i> | Pneumonia (focus of education on national nursing home-acquired pneumonia guidelines)  | RCT (Preintervention period: Nov 1997–April 1998; Postintervention period: Nov 1998–April 1999) <i>Unit of Randomization:</i><br>- SNEs<br><i>Allocation of randomization:</i><br>- Physician-only intervention group<br>- Multidisciplinary intervention group | Ten SNEs from Buffalo, NY, United States (total of 2375 beds)   | <i>Physician-only group:</i><br>- Small-group consensus process for guideline development limited to physicians and nurse practitioners by 2 study physicians<br>- Laminated pocket cards <i>Multidisciplinary group:</i><br>- 1-hour training session on the guidelines for nurses (RNs and LPNs) by 2 study nurses (similar to the small-group consensus conference)<br>- Laminated pocket cards<br>- Laminated posters | - Episodes of pneumonia acquired more than 3 days after admission to SNF<br>- 226 episodes of pneumonia preintervention<br>- 116 episodes of pneumonia post intervention  | <i>Pre- vs Postintervention treatment in accordance with guidelines:</i><br>- IV: 62.2% (79/127) vs 73.4% (47/64), <i>P</i> = .15<br>- Multivariate analysis found significantly more IV use in accordance with guidelines post intervention ( <i>P</i> < .02) PO: 57.6% (57/99) vs 59.6% (31/52), <i>P</i> = .86<br><i>Pre- vs Postintervention IV use in accordance with guidelines by group:</i><br>- Physician-only group: 64.5% (69/107) vs 69% (29/42), <i>P</i> = .73<br>- Multidisciplinary group: 50% (10/20) vs 81.8% (18/22), <i>P</i> = .06<br>- Multivariate analysis found no significant difference in IV use in accordance with guidelines between groups ( <i>P</i> = .13)<br><i>Physician vs multidisciplinary PO use in accordance with guidelines:</i> No difference ( <i>P</i> = .27)<br>- Multivariate analysis found no significant difference in PO use in accordance with guidelines between groups ( <i>P</i> = .27) No differences in 30-day mortality or hospitalization rates between pre- and postintervention groups. |
| Loeb 2005 UTI<br><b>Overall findings:</b><br><i>Educational interventions targeting UTIs decreased overall antimicrobial use</i>                               | Cluster RCT (NHs enrolled from Sept 2001–Feb 2002; last follow-up Mar 2003); <i>Unit of randomization:</i> - NHs <i>Allocation of randomization:</i> - Multifaceted AMS intervention group (intervention group) - Usual care group (control group) | 24 NHs in Ontario, Canada, and Idaho, United States (12 intervention homes, 12 control homes; mean beds 183 ± 64.7)<br>- Multidisciplinary  | - Diagnostic and treatment algorithm for physicians and nurses<br>- Small-group interactive sessions for nurses<br>- Videotapes<br>- Written explanatory materials for physicians<br>- Large posters<br>- Pocket cards<br>- NH staff member assigned to | 20 NHs that completed the study<br>- Included 1896 residents in intervention group<br>- Included 1858 residents in control group  | <i>Intervention vs control homes:</i> Antimicrobials for suspected UTIs/1000 RD: 1.17 vs 1.59 (weighted mean difference -0.49, 95% CI -0.93 to -0.06)<br>- Monthly rates of antimicrobial prescriptions for UTIs were lower in the intervention homes, however nonsignificant trend toward a reduced effect over 12 months (regression coefficient -0.017, 95% CI -0.056 to 0.02)<br>- Proportion of total antimicrobials for suspected UTIs: 28.4% vs 38.6% (weighted mean |  |

| Study: Primary Author and Year of Publication  | Infection of Interest  | Design  | Setting   | Intervention   | Unit of Analysis  | Main Outcomes/Results  |
|--|--|---|---|--|---|--|
| Monette 2007<br><b>Overall findings:</b> <i>When provided with an antibiotic guide and feedback, physicians were less likely to prescribe nonadherent antibiotics.</i> | UTI, SSTI, lower respiratory tract infection, and septicemia of unknown origin | Cluster RCT (Preintervention period: Dec 2001– Feb 2002; Intervention 1: Mar–April 2002; Postintervention period 1: May–July 2002; Intervention 2: Aug 2002; Postintervention period 2: Sept–Nov 2002; Follow-up period: Dec 2002–February 2003) <i>Unit of randomization:</i> LTCFs <i>Allocation of randomization:</i><br>- Physicians who received the intervention (intervention group)<br>- Physicians who provided usual care (control group) | remind nurses to use algorithm<br>- Outreach visits every 3 months<br>- One-on-one interviews with physicians | - Antibiotic guide with feedback on prescribing practices over the previous 3 months mailed to 36 physicians<br>- Intervention repeated 4 months apart | 1539 initial antibiotic prescriptions (1003 intervention, 590 control)  | <i>Change in nonadherent antibiotics pre- to postintervention between intervention vs control homes:</i> 20.5% decrease vs 5.1% decrease <i>Effect of the intervention on the physicians' likelihood of prescribing nonadherent antibiotics with the preintervention period as reference:</i><br>- Postintervention period 1: Intervention physicians 53% less likely to prescribe nonadherent antibiotics (OR 0.47, 95% CI 0.21–1.05)<br>- Postintervention period 2: Intervention physicians 64% less likely to prescribe nonadherent antibiotics (OR 0.36, 95% CI 0.18–0.73)<br>- 15 months follow-up: Intervention physicians 52% less likely to prescribe nonadherent antibiotics (OR 0.48, 95% CI 0.23–1.02) |
| Pettersson 2011<br><b>Overall findings:</b> <i>Educational group sessions with feedback decreased the overall prescribing of antibiotics.</i>                          | All infections   | - Cluster RCT (Preintervention period: Sep–Dec 2003; Intervention Oct 2004–Jan 2005; Postintervention: Feb–May 2005) <i>Unit of randomization:</i> NHs <i>Allocation of randomization:</i><br>- Small educational group sessions with nurses and physicians<br>- Feedback<br>- Presentation of guidelines<br>- Written materials  | 8 public LTCFs in Montreal, Canada (4 intervention LTCFs; 4 control LTCFs)                                    | - Small educational group sessions with nurses and physicians<br>- Feedback<br>- Presentation of guidelines<br>- Written materials                     | 46 nursing homes completed the study<br>- Included 1373 residents in intervention group<br>- Included 1138 residents in control group | <i>Effect of the intervention (95% CI) at 2 years (difference):</i><br>- Proportion of quinolones prescribed for lower urinary tract infection: 0.028 (-0.193 to 0.249)<br>- Proportion of infections treated with antibiotics: -0.124 (-0.228 to -0.019)<br>- Proportion of infections handled by physicians as "wait and see": 0.143 (0.047–0.240)   |

| Study: Primary Author and Year of Publication | Infection of Interest | Design  | Setting | Intervention | Unit of Analysis | Main Outcomes/Results  |
|---|-----------------------|---|---------|--------------|------------------|--|
|   |                       | - Multifaceted AMS intervention group<br>- Usual care group (control group) |         |              |                  | - UTIs per resident: 0.038 (-0.013 to 0.089) No differences in hospital admissions for intervention or control groups. |



**Table 4**  
**Studies to Improve Antimicrobial Use in Long-Term Care Facilities by Type of Intervention**

| Study (Primary Author Year of Publication)  | Infection of Interest  | Design   | Setting   | Intervention  | Unit of Analysis  | Main Outcomes/Results   |
|---|--|--|---|---|---|---|
| <i>Multifaceted Educational Interventions Targeting General Antibiotic Use for All Infection Types.</i> |  |  |   |   |   |   |
| <i>Interventions Targeting Providers Only.</i>  |  |  |   |   |   |   |
| Monette 2007  | See Table 3  |  |   |   |   |   |
| Schwartz 2007   | All infections   | Uncontrolled quasi-experimental study (preintervention period: Jan–Oct 2000; postintervention period: May–Sept 2002) | Public LTC and acute care hospital (340 LTC beds) in Illinois, United States  | - Four educational sessions to 20 internists given by ID specialists (included national guidelines, hospital resistance data, and physician feedback)<br>- Pocket-sized booklets, algorithms, guidelines  | - 200 randomly selected residents treated with antimicrobials (100 preintervention; 100 postintervention) | <i>Antibiotic use compliant with guidelines pre- vs postintervention:</i><br>- Initial treatment agreed with guidelines: 11% vs 39%, $P < .001$<br>- Clinical criteria agreed with guideline diagnostic criteria: 62% vs 32%, $P = .006$<br><i>Interrupted time series analysis of the effect of the interventions on antimicrobial use during the 1.5-year intervention period and 2-year postintervention.</i> Antimicrobial use: Decreased 29.7%; sustained during the postintervention period (ITS demonstrated reduced level and slope during intervention period was significant, $P < .001$ )<br>- Antimicrobial starts: Decreased 25.9%; sustained during the postintervention period (ITS demonstrated reduced level and slope during intervention period but this was not significant) No significant differences in all-cause and infection-related mortality. |
| <i>Interventions Targeting Providers and Nurses.</i>  |  |  |   |   |   |   |
| Pettersson 2011   | See Table 3  |  |   |   |   |   |
| Zimmerman 2014  | UTI, SSTI, respiratory infections, and noninfectious vomiting/diarrhea | Controlled quasi-experimental study (preintervention period: Mar–May 2011, postintervention period: June–Nov 2011)   | 12 NHs in North Carolina, United States (6 intervention NHs [mean beds 146 ± 37.1]; 6 control NHs [mean beds 124 ± 22.2]) | <i>QI program:</i><br>- Educational sessions to providers and nurses by a physician, nurse, ID specialist, and experts in LTC<br>- Medical care referral form and pocket card<br>- Monthly feedback on prescribing to prescribers and nurses<br>- Informational brochure and meetings for nursing home staff, residents, and families | All residents, including 1497 residents treated with antibiotics  | <i>Effect of intervention on antibiotic prescribing rates between pre- and postintervention periods for intervention vs control NHs:</i><br>- Total antibiotics for all infections: IRR 0.86, 95% CI 0.79–0.95, $P < .05$<br>- Antibiotics for respiratory infections: IRR 0.71, 95% CI 0.56–0.90, $P < .05$<br>- Antibiotics for UTIs: IRR 0.84, 95% CI 0.66–1.05, $P > .05$<br>- Antibiotics for SSTI: IRR 0.89, 95% CI 0.62–1.28, $P > .05$  |

| Study (Primary Author Year of Publication)   | Infection of Interest   | Design  | Setting   | Intervention  | Unit of Analysis   | Main Outcomes/Results  |
|--|---|---|---|---|--|--|
| <b>Multifaceted Educational Interventions Targeting Antibiotic Use for Pneumonia.</b>  |   |   |   |   |  |  |
| Naughton 2001  | See Table 3   |   |   |   |  |  |
| Hutt 2006<br><b>Overall findings:</b> Educational sessions and academic detailing for pneumonia not associated with significant improvements in antibiotic choice or timing in intervention homes. | Pneumonia (focus of education on national nursing home-acquired pneumonia guidelines) | Controlled quasi-experimental study (preintervention period: Nov 2003–Apr 2004, postintervention period: Nov 2004–Apr 2005)                       | Two state veterans homes in Colorado, United States (1 intervention NH [134 beds]; 1 control NH [120 beds])           | <ul style="list-style-type: none"> <li>- Interactive educational sessions for nurses</li> <li>- Toolkit (annotated copy of guidelines, case studies, preprinted orders, pocket card with guideline reminders, and posters) disseminated throughout facility</li> <li>- Academic detailing to physicians and providers</li> </ul>                  | 86 residents with 2 or more signs of lower respiratory tract infections (46 intervention group; 40 control group)  | <p><i>Change in guideline compliant antibiotics pre- to postintervention in intervention homes:</i></p> <ul style="list-style-type: none"> <li>- Antibiotic choice: 63% vs 81%, <math>P &lt; .05</math></li> <li>- Timely antibiotic: 88% vs 79%, <math>P &gt; .05</math></li> </ul> <p><i>Guideline-compliant antibiotics in intervention homes vs control homes during postintervention period:</i></p> <ul style="list-style-type: none"> <li>- Antibiotic choice: 81% vs 33%, <math>P &lt; .05</math></li> <li>- Timely antibiotic: 79% vs 17%, <math>P &lt; .05</math></li> </ul> <p>No significant differences in mortality or hospitalization rates between intervention and control groups.<br/>No significant differences in mortality or hospitalization rates between pre and post periods.</p> |
| Linnebur 2011<br><b>Overall findings:</b> Educational sessions and academic detailing or pneumonia improved timing but not choice of antibiotics.  | Pneumonia (focus of education on national nursing home-acquired pneumonia guidelines) | Controlled quasi-experimental study (preintervention period: Oct 2004–Apr 2005, postintervention period: Oct 2005–Apr 2006 and Oct 2006–Apr 2007) | Sixteen NHs in Colorado (8 intervention NHs [mean beds 134] and Kansas, United States (8 control NHs [mean beds 128]) | <ul style="list-style-type: none"> <li>- Educational sessions for nurses</li> <li>- Academic detailing to prescribers by pharmacists regarding diagnostic and prescribing practices</li> </ul>  | 1,123 episodes of pneumonia evaluated (549 intervention group; 574 control group)  | <p><i>Difference in change pre- and postintervention of antibiotic use compliant with guidelines between intervention vs control homes:</i></p> <ul style="list-style-type: none"> <li>Antibiotic choice: 6% increase vs 7% increase, <math>P = .3</math></li> <li>Antibiotic duration: 14% decrease vs 5% increase, <math>P &gt; .05</math></li> <li>Timely antibiotic: 18% increase vs 7% decrease, <math>P = .0003</math></li> </ul> <p>No significant differences in mortality between intervention and control groups.</p>  |
| <b>Multifaceted Educational Interventions Targeting Antibiotic Use for Suspected Urinary Tract Infections.</b>   |   |   |   |   |  |  |
| Loeb 2005  | See Table 3   |   |   |   |  |  |
| Zabarsky 2008<br><b>Overall findings:</b> Educational sessions with feedback for ASB decreased treatment for ASB and inappropriate urine cultures.   | ASB   | Uncontrolled quasi-experimental study (preintervention period: 3 months, postintervention period 30 months; Feb 2002–Oct 2004)                    | VA Medical Center in Cleveland, Ohio, United States (190 LTC beds)  | <ul style="list-style-type: none"> <li>- Educational sessions to nurses and providers conducted by an IC nurse and ID physician</li> <li>- Pocket-sized reference cards, larger cards at each computer station</li> <li>- Semiannual follow up educational sessions</li> <li>- Individualized direct feedback for nurses and providers</li> </ul> | <p><i>Pre-Intervention vs. 6 months post and vs. 30 months post:</i></p> <ul style="list-style-type: none"> <li>Antibiotic regimens for ASB: 68% vs 69%, <math>P = .90</math> vs 44%, <math>P = .022</math></li> <li>ASB treated/1000 PD days: 1.7 → 0.6 (IRR 0.37, 95% CI 0.19–0.72, <math>P = .002</math>) → 0.3</li> <li>Total antibiotic days DOT/1000 PD: 167.7 → 117.4 (<math>P &lt; .001</math>) → 109 (<math>P &lt; .001</math>)</li> <li>Inappropriate cultures: 69% vs 61% vs 46%</li> </ul> |  |

| Study (Primary Author Year of Publication)   | Infection of Interest | Design   | Setting   | Intervention   | Unit of Analysis   | Main Outcomes/Results  |
|--|-----------------------|--|---|--|--|--|
| Rummukainen 2013<br><b>Overall findings:</b><br><i>Academic detailing decreased proportion of residents on antibiotic prophylaxis for UTI.</i>             | UTI prophylaxis       | Uncontrolled pre-(2005 baseline visit) vs post (2006, 2007, 2008) surveys  | 25 primary care hospitals and 39 NHs in Finland   | - Academic detailing to head practitioners and head nurses (by an ID consultant, IC nurse, and geriatrician)<br>- Regional guidelines<br>- Annual surveys to reinforce guidelines  | Inappropriate cultures sent/1000 PD:<br>2.6 → 0.9 (IRR 0.36, 95% CI 0.21–0.62, $P < .001$ ) → 0.6<br><br>68 units visited and responded to surveys   | <i>The proportion of residents on antibiotic prophylaxis for UTI: 14.5% in 2005 to 7.8% 2008, <math>P &lt; .001</math></i>   |
| Trautner 2015<br><b>Overall findings:</b><br><i>Educational sessions, feedback, and a diagnostic algorithm targeting ASB reduced overtreatment of ASB.</i> | ASB                   | Controlled quasi-experimental study (preintervention period: July 2010–June 2011; intervention period: July 2011–June 2012; maintenance period: July 2012–June 2013)     | Two VA Health Care System Medical Centers in Texas, United States (intervention center in Houston and 5 LTC wards included), 1 control center in San Antonio [3 general medicine and 2 LTC wards included]; United States | - CAUTI vs ASB diagnostic algorithm<br>- Case-based individualized audit and feedback to train clinicians to use algorithm<br>- Educational sessions to practitioners and nurses by principal investigator (MD, PhD)       | <i>LTC Residents Only:</i><br>Overtreatment of ASB lower during the intervention (OR 0.23, 95% CI 0.08–0.65) and maintenance (OR 0.10, 95% CI 0.01–0.84) periods at the intervention facility.<br>Overtreatment of ASB higher during the intervention (OR 9.67, 95% CI 1.43–65.38) and similar for the maintenance (OR 3.45, 95% CI 0.61–19.53) periods at the control facility. <i>All subjects:</i> Significant decrease in the number of urine cultures ordered per month over time when comparing 2 sites ( $P < .001$ ) |  |
| <b>Implementation of a Novel Antimicrobial Stewardship Tool.</b>   |                       |  |   |  |  |  |
| Fleet 2014<br><b>Overall findings:</b><br><i>Antimicrobial stewardship tool decreased antibiotic use and improved appropriate treatment.</i>               | All infections        | Cluster RCT (preintervention period: Jan–May 2010; postintervention period: Jan–May 2011 post)<br><i>Unit of randomization:</i><br>- NHs<br>Allocation of randomization: | 30 NHs in London, England (15 intervention NHs, 15 control homes [total of 1832 beds in both groups])   | - Antimicrobial stewardship tool (preprinted form) for nurses<br>- Support pack for nursing staff and managers<br>- Dedicated telephone number for the project<br>- Follow-up visits<br>- Posters and promotional material | 3328 residents (1665 intervention, 1575 control)   | <i>Intervention vs control homes:</i> Change in total antibiotic consumption pre vs post: 4.9% decrease (3.25 DDD/1000 RD, 95% CI 1.0%–8.6%, $P = .02$ , intervention group)<br>5.1% increase (2.42 DDD/1000 RD, 95% CI 0.2%–10.2%, $P = .04$ , control group)<br>Change in total antibiotic consumption for prophylaxis pre vs post: 2.72 DDD/1000 RD decrease (intervention group) |

| Study (Primary Author Year of Publication)  | Infection of Interest | Design   | Setting   | Intervention   | Unit of Analysis  | Main Outcomes/Results  |
|---|-----------------------|--|---|--|---|--|
|   |                       | - AMS Tool group (intervention group)<br>- Usual care group (control group)  |   |  |   | 0.83 DDD/1000 RD increase (control group)<br><i>Proportion of residents that fully met "McGeer Criteria" postintervention between intervention vs control homes: 11.1% vs 2.6%, P = .004 (estimated relative increase 6.44)</i><br><i>Proportion of residents that fully met "Loeb minimum Criteria" postintervention between intervention vs control homes: 19.3% vs 5.1%, P = .001</i><br>No ADEs due to tool. |
| <b>Implementation of an Infectious Diseases Consultation Service.</b>   |                       |  |   |  |   |  |
| Jump 2012 Overall findings: ID consult service decreased antibiotic use and of rate of positive C difficile tests | All infections        | Uncontrolled quasi-experimental study (pre-ID service period: July 2006–June 2009, post-ID service period: July 2009–Dec 2010) | VA LTCF in United States (160 beds)   | ID consult service that consisted of an ID physician and a nurse practitioner who examined residents at the LTCF once each week and the remainder of the week were available for remote consultation (via telephone and the electronic medical record) | Antibiotic DOT/1000<br>DOC C difficile tests/<br>1000 DOC | <i>Pre- vs post-ID consult:</i><br>- Total systemic antibiotic mean DOT/1000 DOC: 175.1 vs 122.3, <i>P</i> < .001 (30.1% decrease)<br>- Rate of positive C difficile tests declined in the post-period relative to preperiod rates, <i>P</i> = .04<br>- Hospital transfers per month: 19.0 vs 17.6, <i>P</i> = .27   |
| <b>Implementation of an Antibigram.</b>   |                       |  |   |  |   |  |
| Furuno 2014 Overall findings: Antibigram nonsignificantly increased appropriate empiric prescribing.              | All infections        | Uncontrolled quasi-experimental Study (pre-antibigram period: 6 months, post-antibigram period: 6 months)                      | Three SNFs in Maryland, United States (antibigram effectiveness assessed a single SNF [118 beds]) | - Antibigram<br>- Educational in-services (introduction of the antibigram and explanation of how to use the tool) to nursing staff, administrators, nurse managers, and physicians by study staff  | 839 resident charts reviewed to inform the antibiograms   | <i>Pre- vs. Post-antibigram prevalence of appropriate empiric antibiotic prescribing: 32% vs 45%, P = .32</i>  |