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Review Article

Antibiotic Stewardship Programs in Nursing Homes: A Systematic Review

Diana Feldstein MD, MPH [a,*], Philip D. Sloane MD, MPH [b,c], Cynthia Feltner MD, MPH [c,d]

[a] Division of Geriatric Medicine, Center for Aging and Health, University of North Carolina, Chapel Hill, NC
[b] Department of Family Medicine, University of North Carolina, Chapel Hill, NC
[c] Cecil G. Sheps Center for Health Services Research, University of North Carolina, Chapel Hill, NC
[d] Department of Medicine, University of North Carolina, Chapel Hill, NC

A B S T R A C T

Introduction: Antibiotic stewardship programs (ASPs) are coordinated interventions promoting the appropriate use of antibiotics to improve patient outcomes and reduce microbial resistance. These programs are now mandated in nursing homes (NHs) but it is unclear if these programs improve resident outcomes. This systematic review evaluated the current evidence regarding outcomes of ASPs in the NH.
Methods: PubMed, CINAHL, EMBASE, and the Cochrane Library were systematically searched for intervention trials of ASPs performed in NHs that evaluated final health outcomes (mortality and *Clostridium difficile* infections), healthcare utilization outcomes (emergency department visits and hospital admissions) and intermediate health outcomes (number of antibiotics prescribed, adherence to recommended guidelines).
Results: A total of 14 studies rated good or fair quality were included. Eight studies reported a reduction in antibiotic prescriptions. Ten found an increase in adherence to guidelines proposed by the studied ASP. None reported a statistically significant change in NH mortality rates, *C. difficile* infection rates, or hospitalizations.
Discussion: The limited research to date suggests that NH ASPs can affect intermediate health outcomes, but not key health outcomes or health care utilization.
Conclusion: Larger trials evaluating more intensive interventions over longer durations may be needed to determine whether ASPs in NHs improve health outcomes as they have in hospitals.

The 1.4 million older adults residing in American nursing homes (NHs)[1] are at a particularly high risk of multidrug-resistant organism (MDRO) infection due to antibiotic overuse.[2] It is estimated that 1 in 3 NH residents are colonized with an MDRO and that as many as 75% of the 3 million annual antibiotic prescriptions for presumed infections in NH residents may be inappropriate.[3–5] MDRO infections are difficult to treat and require broad-spectrum antibiotics, thereby increasing the risk of potentially fatal *C. difficile* infections (CDI).[6] The tremendous cost and risk of CDI and other adverse events associated with antibiotic overuse has led to calls for a more judicious approach to antibiotic prescribing[7–9] via antibiotic stewardship programs (ASPs)—coordinated efforts promoting the optimal use of these powerful medications throughout all healthcare settings, including NHs.[10]

NH residents present unique challenges for antibiotic stewardship. The multiple comorbidities typical of NH residents,[11] combined with the aging immune system, lead to atypical and often subtle changes in the presentation of bacterial infections.[12] More than half of the current NH population has some degree of functional impairment and needs assistance in many or all of the activities of daily living (including bathing, toileting, dressing, ambulation, feeding).[1,13] This leads to high levels of intimate contact between staff and residents, which contributes to the spread of MDROs from person to person.[2] Furthermore, the majority of NH residents have sufficient cognitive impairment to limit their ability to communicate a coherent history,[14] and this can lead to antibiotic prescriptions for nonspecific symptoms that are not necessarily caused by bacterial infections.[15] In addition, frail NH residents are hospitalized more frequently than an age-matched cohort,[16] increasing their exposure to even more MDROs.

The typical NH has limited resources to diagnose acute bacterial infections, such as diagnostic testing or imaging.[5] NHs often have staff-to-resident ratios that are orders of magnitude lower than those

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* Address correspondence to Diana Feldstein, MD, MPH, Providence Elder at Home, 4900 NE Gilsan Street, Portland, OR 97213.
E-mail address: diana.feldstein@providence.org (D. Feldstein).

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of hospitals,[17] which may lower the quality of care.[18] Medical equipment is shared between caregivers and residents, also contributing to the rapid spread of MDROs in this environment.[19] Not surprisingly, then, the risk of colonization with MDROs is especially high in residents with in-dwelling devices such as urinary catheters.[20]

Recognizing these challenges, specific guidelines for infection surveillance and treatment recommendations in the NH have been published.[21,22] However, these guidelines are largely based on expert opinion, as there is limited empirical research on management of infections in the NH. Furthermore, published guidelines do not appear to be used regularly to guide NH infection management.[23–25] Rather than using these guidelines, providers appear to rely on diagnostic tests such as urinalyses or chest radiographs when an infection is suspected. Although these results may not provide evidence of an infection, they more often increase antibiotic prescribing.[24,26,27]

Hospital-based ASPs have been successful at reducing potentially inappropriate prescribing.[10] ASPs are now mandated in American NHs,[9] but it is unknown what aspects of these programs are effective in this setting. To assess the potential benefit of ASPs in NHs, we conducted a systematic review. Our main study questions involved whether these programs lead to improved health outcomes and lower rates of health care utilization.

Methods

To evaluate the impact of ASPs on health outcomes, we sought to determine if ASPs in the NH reduced mortality and/or reduced the incidence of CDI. To evaluate ASPs' impact on health care utilization, we focused on emergency department visits for a suspected bacterial infection (sepsis, pneumonia, urinary tract infection [UTI], or cellulitis) and hospitalizations (overall and for bacterial infections). We also sought to evaluate the impact of ASPs on the following intermediate health outcomes: changes in the rates of antibiotic prescriptions and the proportion of antibiotic prescriptions that were concordant with guidelines.

Data Sources and Searches

PubMed/MEDLINE, the Cochrane Library, EMBASE, and CINAHL were searched for relevant English-language articles from database inception through February 2017. Medical Subject Headings were used as search terms when available and keywords when appropriate, focusing on terms that describe relevant populations, interventions, and study designs. Complete search terms and limits are listed in Appendix A. Targeted searches were used for unpublished literature by searching ClinicalTrials.gov and the WHO International Clinical Trials Registry Data Platform. To supplement electronic searches, reference lists of pertinent review articles were examined, and studies that met the inclusion criteria were added to potentially relevant articles.

Study Selection

We included English-language randomized controlled trials, nonrandomized trials and observational studies of eligible interventions in adults age 65 years or older conducted in countries categorized as "very high" on the Human Development Index.[28] We excluded studies of patients with active cancer, HIV/AIDS, end-stage renal disease requiring hemodialysis, organ transplant recipients, and other conditions that directly cause or require immunosuppression, thereby changing antibiotic treatment and prophylaxis practices.

Cluster randomized controlled trials comparing NHs with ASPs to those without were eligible. Nonrandomized controlled trials and observational studies were also acceptable given the limited literature on this topic. Studies with a comprehensive ASP were included, but not studies assessing interventions focused on one single component of an ASP, such as hand hygiene.

Titles and abstracts of all publications identified were reviewed against prespecified inclusion criteria. All full texts of abstracts that appeared relevant were reviewed to determine final eligibility.

Quality Assessment and Data Abstraction

For each included study, we extracted pertinent information about the methods, populations, interventions, comparators, outcomes, timing, settings and study design. We then assessed the quality of the included studies as good, fair, or poor using predefined criteria developed by the National Institutes of Health for RCTs[29] and nonrandomized interventional studies[30] as seen in Appendix B. We included only studies rated as having good or fair quality.

Data Synthesis and Analysis

We qualitatively synthesized findings by summarizing the characteristics and results of included studies in tabular and narrative format. Meta-analysis was not appropriate because of heterogeneity across studies in terms of intervention type, outcomes, and study design.

Results

We identified 592 unique titles and abstracts and assessed 29 full-text articles for eligibility (Figure 1). We excluded 15 articles for various reasons detailed in Appendix C and included 14 published studies of good or fair quality.[31–44] These included 5 cluster randomized controlled trials,[32,37,39–41] 3 controlled before-after trials,[34,36,42] 4 before-after trials without controls,[31,33,35,43] and 2 nonrandomized controlled trials.[38,44]

Characteristics of included studies are summarized in Table 1. All included studies used the individual NH as unit of intervention allocation; sample sizes ranged from 1 NH to 58 NHs. Eleven of the 14 studies reported the residents of participating NHs as study subjects, but, in reality, only 4 studies treated the individual NH resident as a study subject,[33,34,36,40] with the remainder analyzing antibiotic prescriptions as the unit of intervention. Ten studies were set in the United States and one each in the United Kingdom,[32] Sweden,[41] the Netherlands,[42] and Canada.[37]

There was significant heterogeneity in terms of intervention components and delivery personnel. Most studies included some aspect of an educational lecture to NH staff and physicians. One study included 2 arms: a physician-only arm and a multidisciplinary arm including physicians and nurses.[40] Two used an infectious disease consultant team that directed recommendations exclusively to NH prescribers; 3 used an intervention that included NH prescribers and nursing staff[37,40–43]; and 1 included residents and families as well as prescribers and nurses.[44] The comparators were generally usual care (ie, no formal ASP). The outcomes of interest included final health outcomes (mortality or CDI), healthcare utilization outcomes (emergency department visits, hospitalizations), and intermediate healthcare outcomes (decreased antibiotic use, improved guideline adherence). The longest studies were 36 months.[34,36] Quality assessments of the included studies are presented in Appendix B.

Impact of ASPs on Health Outcomes and Health Care Utilization

Four studies measured mortality following institution of ASPs in NHs.[34,35,37,40] Loeb et al did not find a significant difference in morality between intervention homes and controls (1.11 per 1000 resident days in the intervention arm compared with 1.09, weighted mean difference 0.07, −0.22 to 0.36).[37] Naughton et al similarly did not find a difference in mortality, with a mortality of 23.9% in intervention