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REVIEW ARTICLE

Optimizing Antibiotic Stewardship in Nursing Homes: A Narrative Review and Recommendations for Improvement

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Abstract The emerging crisis in antibiotic resistance and concern that we now sit on the precipice of a post-antibiotic era have given rise to advocacy at the highest levels for widespread adoption of programmes that promote judicious use of antibiotics. These antibiotic stewardship programmes, which seek to optimize antibiotic choice when clinically indicated and discourage antibiotic use when clinically unnecessary, are being implemented in an increasing number of acute care facilities, but their adoption has been slower in nursing homes. The antibiotic prescribing process in nursing homes is fundamentally different from that observed in hospital and clinic settings, with formidable challenges to implementation of effective antibiotic stewardship. Nevertheless, an emerging body of research points towards ways to improve antibiotic prescribing practices in nursing homes. This review summarizes the findings of this research and presents ways in which antibiotic stewardship can be implemented and optimized in the nursing home setting.

Key Points

The antibiotic prescribing process in nursing homes is complex and differs from the prescribing process in hospital and clinic settings.

Improvements in the quality of antibiotic prescribing in nursing homes have been achieved through a variety of antibiotic stewardship interventions.

Implementing and sustaining antibiotic stewardship in nursing homes requires an organizational commitment and a strategy based on goal setting, process and outcome measurement, and continuous quality improvement.

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> It is not difficult to make microbes resistant to penicillin … The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily under dose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant.
>
> -Alexander Fleming's Nobel Prize Acceptance Lecture, 1945

1 Introduction

The discovery of penicillin in 1928, followed by its commercialization in the 1940s, ushered in the antibiotic era of medicine [1]. During that time, unparalleled advances in health care were achieved, largely through a new-found capacity to eradicate infections associated with disease states that had previously rendered their treatment unthinkable. Nevertheless, excessive use of antibiotics in the ensuing decades, coupled with underinvestment in discovery and development of new agents, has culminated in a crisis of antibiotic resistance [2], which, if left unchecked, will have catastrophic consequences for patients and the economy [3]. In response, specialty societies [4] and governmental authorities [5, 6] have advocated for a substantial increase in antibiotic stewardship activity across the health care continuum. To date, efforts to implement these antibiotic stewardship programmes (ASPs)—which are defined as coordinated efforts to optimize patient outcomes and reduce the emergence and spread of antibiotic resistance through promotion of appropriate antibiotic use—have focused on the hospital setting. However, as is described below, the need for similar efforts in nursing homes (including the care of short-stay residents with skilled nursing and rehabilitation needs, as well as long-stay residents) may be even greater. Fortunately, a considerable number of studies focused on improving antibiotic prescribing in nursing homes have been published in recent years. Consequently, the primary aims of this paper are to review the current literature on antibiotic stewardship in nursing homes and provide recommendations that facilities can implement in order to improve existing antibiotic prescribing patterns.

2 The Need for Antibiotic Stewardship in Nursing Homes

While the numbers vary by country, approximately 2–5 % of the developed world's older population resides in some type of long-term care facility [7, 8]. For example, nearly 1.4 million persons reside in the 15,700 nursing homes in the USA [9]. Similar proportions of the populations in Canada [10] and the UK [11] reside in this type of facility. Residents in these facilities are predominantly frail and prone to developing infections. In fact, infections are the most common cause of transfers to acute care and a major source of nursing home resident morbidity and mortality [12, 13]. Against this backdrop, it is not surprising that antibiotics are among the most commonly prescribed medications in nursing homes [14]. On average, one in ten nursing home residents is receiving antibiotics on any given day [15–17]. For the resident who remains in a nursing home for at least 6 months, this translates into a 40–70 % likelihood of exposure to at least one course of antibiotics [14, 18].

While antibiotics are undoubtedly beneficial in many situations, they are not uniformly benign or helpful. Antibiotics pose a risk of adverse side effects similar to that seen with antipsychotic medications [19] and account for nearly 20 % of the adverse drug events observed in nursing homes [20]. A resident's risk of developing *Clostridium difficile* infection (CDI), an increasingly common problem encountered in nursing homes [21, 22], is amplified eightfold following treatment of a suspected urinary tract infection (UTI) [23]. Antibiotics also substantially increase a resident's risk of acquiring antibiotic-resistant bacteria [24], which may result in subsequent infections that are more expensive to treat [25] and are more likely to produce adverse health outcomes [26–28]. Residents who become colonized with antibiotic-resistant bacteria following exposure to antibiotics may also spread these organisms to other residents in the nursing home [29–32] and to individuals in other health care settings during care transitions [33]. It is increasingly clear that a substantial number of these resident harms could be avoided through improvements in antibiotic prescribing practices in nursing homes.

Prospective studies have shown that nearly half of the antibiotic courses prescribed in nursing homes are unnecessary [18, 23, 34–37]. Even when clinically indicated, the antibiotic prescribed very often is excessively broad spectrum or is continued for a duration well beyond what is required to eradicate the infection. Fluoroquinolones are the most commonly prescribed class of antibiotics in US and Canadian nursing homes, accounting for 38 and 23 % of total antibiotic use, respectively [14, 17]. However, most of the infections encountered in nursing homes can be treated with alternative agents that pose lesser risks of side effects and CDI [23, 35]. Despite a number of studies demonstrating the safety and benefits of short-course antibiotic therapy [38–40], more than 60 % of the residents treated for nursing home infections receive antibiotics for more than a week and nearly a third are treated for more than 10 days [17].

3 The Antibiotic Prescribing Process

Progress towards improving antibiotic prescribing practices in nursing homes requires an understanding of the decision-making involved. Antibiotic prescribing is best viewed as a process rather than a discrete event (Fig. 1) [41]. Conceptually, this process begins with a decision to initiate an antibiotic, as well as a related decision about which antibiotic(s) to prescribe. The initial decision to prescribe is influenced by a number of factors (Fig. 2) [42–46], although the relative influences of these factors vary not only from case to case but also depending on the country. For example, family preferences exert a considerable influence over prescriber decision-making in US, Canadian and Australian nursing homes [42, 43, 45, 47] but appear to minimally impact prescribing decisions in Dutch nursing homes [44].

In many nursing homes, the initial decision to prescribe an antibiotic is made off-site by telephone and, therefore, is heavily influenced by nursing home staff and inter-professional communication [42, 43, 47]. Decisions are often based on limited laboratory and clinical information, so clinicians frequently prescribe broad-spectrum agents to enhance coverage for a range of potential pathogens [45, 46]. Ideally, these same clinicians should then reassess the patient several days later to decide if the empirical antibiotic regimen can be de-escalated (Fig. 1). Consistent application of post-prescribing review and de-escalation, which is sometimes referred to as an 'antibiotic timeout' [48], allows the clinician to maximize the benefits of antibiotics while minimizing their adverse effects [49]. This antibiotic timeout should involve review of accumulated laboratory and imaging studies, as well as a re-evaluation of the patient's status since initiating the antibiotic. If the data suggest a non-infectious cause for the patient's illness, the antibiotic should be stopped. Conversely, if these data point towards infection, then clinicians should use the available culture results and observed changes in the patient's clinical status to select a definitive antibiotic regimen that possesses the narrowest possible spectrum and is given for the shortest possible duration.

4 Barriers to Improving Antibiotic Use in Nursing Homes

The underlying frailty of most nursing home residents engenders a high level of risk aversion among providers who deliver care in the nursing home setting [46]. Immunosenescence and multimorbidity, both of which increase a resident's risk of infection, are the norm in nursing homes [50, 51]. Reduced skin integrity and exposure to invasive medical devices, such as indwelling urinary catheters and feeding tubes, further compromise intrinsic host immunity [52–54]. Even when infection is identified and treated promptly, a resident's risk of experiencing adverse outcomes, such as hospitalization and death, remains high.

Diagnosis of infection in aging populations remains a challenge. Among older adults, temperature elevation (or decline/depression) in response to infection is often blunted. Cognitive impairment, which afflicts >50 % of nursing home residents, makes it difficult for residents to vocalize and/or localize their symptoms [55–59]. While nursing homes have the capacity to perform common laboratory tests, most rely upon off-site facilities for this service. Consequently, even basic laboratory test results tend to be reported a day or more after they are ordered, and culture results take even longer. Moreover, while most nursing homes have access to mobile radiographic services, the image quality may be suboptimal [60].

The unique structure of resident evaluation and treatment in nursing homes may represent the most important barrier to improving antibiotic stewardship. While an increasing number of providers in the USA and some other countries practice primarily in the nursing home setting [61, 62], the majority of care in nursing homes is delivered by providers who, on average, physically spend less than 2 h per week in a nursing home [63, 64]. Consequently, most antibiotic decisions are made by off-site providers during brief telephone interactions with facility nursing staff [65, 66]. This process relies heavily on certified nursing assistants (CNAs) and licensed nursing staff. A CNA is frequently the first individual to recognize a

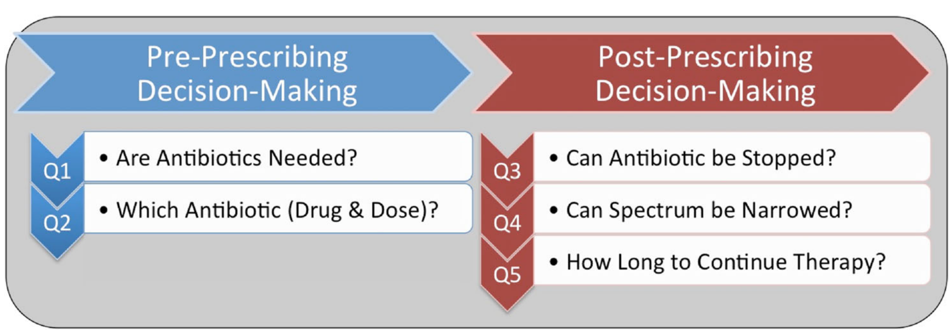

Fig. 1 Components of the antibiotic prescribing decision-making process

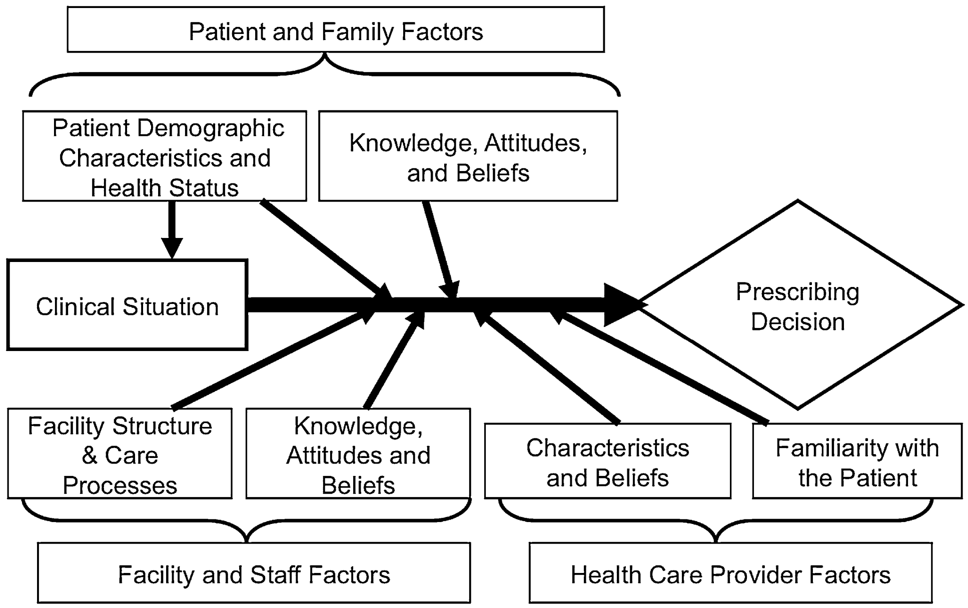

Fig. 2 Conceptual framework of the factors that influence the decision to initiate antibiotic therapy in nursing homes

resident's change in condition and can play a critical role in assisting nursing staff in evaluation of the resident. However, resources devoted to the training of these individuals is often minimal, and retention of experienced individuals continues to be a challenge for many nursing homes [67, 68]. Accordingly, a registered nurse (RN) or licensed practical nurse (LPN) must not only complete the initial assessment and examination of a resident with a change in condition but also communicate those findings to the provider on call. The nurses' workload and familiarity with the residents influence this process. Unfortunately, nurse-to-resident ratios [69] and consistent assignments remain suboptimal in many nursing homes [70]. Moreover, a high reliance on agency staff [69], as well as high levels of staff turnover [71], further compound the problem. It is, therefore, not surprising that providers often express frustration over the quality of information received during their telephone interactions with nursing home staff [72–74]. The clinical uncertainty engendered by these assessment and communication processes may, in part, lower the threshold at which providers decide to prescribe an antibiotic [75, 76].

5 Existing Studies of Antibiotic Stewardship in Nursing Homes

A loose definition of antibiotic stewardship encompassing interventions to alter antibiotic prescribing patterns in nursing homes, including decisions to initiate antibiotic therapy, as well as the choice and duration of therapy, was employed in the development of this review. A formal systematic review process was not employed in the identification and quality assessment of the studies considered in this review. However, the lead author (CJC) did conduct a search of PubMed articles available as of April 2015, reviewed citation lists from the retrieved review articles [77–79] and further reviewed abstracts and presentations at pertinent international scientific meetings (e.g. IDWeek) in order to identify potential studies for review. Co-authors contributed to the identification of additional articles not identified by this initial retrieval process and also participated in the interpretation of individual study findings, which were then synthesized through group consensus. This process led to the identification of 14 studies focused on altering antibiotic prescribing practices in nursing homes (Table 1). Most of the interventions described in these studies focused on empirical prescribing decision-making through interventions to either reduce initiation of unnecessary antibiotics (Q1 in Fig. 1) [80–87] or enhance adherence to antibiotic prescribing guidelines (Q2 in Fig. 1) [81, 83, 88–91]. The impacts of these interventions on measured outcomes varied considerably across studies. Nevertheless, review of the studies in aggregate points to several promising strategies.

5.1 UTI-Focused Interventions

The most common indication for initiation of antibiotics in nursing homes is UTI [14, 36, 92, 93]. Nevertheless, most residents treated for UTI do not manifest symptoms that are localized to the urinary tract [56]. Rather, studies suggest that a substantial number of these events represent unnecessary treatment of asymptomatic bacteriuria [58, 94].

Vague symptoms that have no clear relationship to the urinary tract, such as malaise or falls, are often cited as a reason to test resident urine samples [56]. Unfortunately, urine diagnostic tests—including the rapid urine reagent strip (dipstick), urinalysis and urine culture—fail to discriminate between UTI and asymptomatic bacteriuria [95–97]. Nonetheless, there is compelling evidence that positive urine test results play an inordinate role in the decision to initiate an antibiotic [94]. For example, 60–90 % of the antibiotics prescribed for UTI in nursing homes are initiated only after urine cultures results are available [56, 98]. Moreover, withholding urine culture results, unless specifically requested by the provider, substantially reduces the frequency of antibiotic starts in hospitals without adversely affecting patient outcomes [99].

On the basis of these observations, it is reasonable to hypothesize that antibiotic prescribing for UTI can be reduced through interventions that target over-testing of resident urine samples. The first large-scale study to test this hypothesis employed criterion-based pathways to limit urinary testing and antibiotic prescribing to residents with fever and/or localizing urinary symptoms [80]. This study, performed in 24 nursing homes in the USA and Canada, demonstrated a reduction in antibiotic prescribing for UTI (1.17 versus 1.59 antibiotic starts per 1000 resident-days), but the effects waned over time, and there was a non-significant impact on orders for urine cultures (2.03 versus 2.48 cultures per 1000 resident-days), suggesting issues with intervention sustainability and fidelity [100]. Nevertheless, a subsequent study in a single Veterans Affairs (VA) nursing home demonstrated an impressive reduction in urine cultures (1.5 versus 3.7 cultures per 1000 resident-days), treatment of asymptomatic bacteriuria (0.6 versus 1.7 courses per 1000 resident-days) and overall days of antibiotic therapy (117 versus 168 days per 1000 resident-days) following implementation of the same intervention [82]. Similarly, treatment of asymptomatic bacteriuria was reduced from 52 to 10 % ($P = 0.001$) following implementation of a cognitive intervention [101] focused on limiting urine cultures in residents with guideline discordant symptoms (e.g. foul-smelling urine) [87]. Finally, significant reductions in urine cultures [incidence rate ratio (IRR) 0.73; 95 % confidence interval (CI) 0.66 to 0.79] and antibiotic therapy for UTI (IRR 0.67; 95 % CI 0.59–0.76) were achieved following implementation of a quality improvement collaborative focused on improving urine testing in 17 Massachusetts nursing homes [86].

5.2 Standardized Assessment and Communication Interventions

Despite the availability of guidelines [102], there is evidence that assessments of residents with possible infection are suboptimal in many nursing homes [18, 34, 65]. Even when the assessment is thorough, the quality of the communication between facility nursing staff and providers, which has been previously linked to use of antipsychotics [103] and avoidable hospitalizations [73, 104], may be suboptimal. While the linkage between communication and antibiotic prescribing is less clear [42], interventions structured around standardizing resident assessments and interdisciplinary communication have led to reductions in antibiotic use in nursing homes [84, 85]. A medical provider and nurse-based intervention—which included training on antibiotic stewardship, a simple form that facilitated standardization of communication with providers and an informational brochure for families and residents—led to lower overall antibiotic prescribing in comparison with control facilities (IRR 0.86; 95 % CI 0.79–0.95) [85]. Similarly, antibiotic prescribing in Texas nursing homes was 33 % lower in nursing homes that implemented a standardized communication and UTI decision-support form with high fidelity in comparison with control nursing homes and facilities that implemented the form with low fidelity [84].

5.3 Educational Interventions

Education can be an effective behavioural intervention in situations where knowledge deficiencies drive observed practice patterns [105]. The available studies suggest that educational interventions have a modest impact on antibiotic use in nursing homes. The number of antibiotic starts dropped by 26 % and days of antibiotic therapy were reduced by 30 % following implementation of a case-based educational intervention focused on treatment of commonly encountered infections in a Chicago long-term care facility [81]. The impact of educational interventions when delivered across multiple facility settings has been less impressive. A cluster-randomized study of an educational intervention to improve adherence to a prescribing guideline in Canadian nursing homes demonstrated improvements in provider guideline adherence rates, but this difference did not remain significant during long-term follow-up [89]. Similarly, a cluster-randomized study of an educational intervention to reduce fluoroquinolone utilization in Swedish nursing homes did not demonstrate a significant impact on this particular prescribing pattern, although the proportion of infections treated with antibiotics was lower in intervention nursing homes compared with control facilities (difference-in-differences of proportions −0.124; 95 % CI −0.228 to −0.019) [83]. Interestingly, the effectiveness of educational interventions may rely on simultaneous delivery of content to facility nursing staff and prescribing providers. A cluster-randomized trial of an educational intervention to improve antibiotic

Table 1 Summary of antibiotic stewardship intervention studies in long-term care facilities

References	Study characteristics	Interventions	Outcomes
Naughton et al. [88]	Design: cluster-randomized study in 10 NHs Focus: NH-acquired pneumonia Randomization: 5 NHs allocated to an educational intervention targeted at prescribers only (5 NHs) and 5 NHs allocated to an educational intervention targeted at prescribers and nursing staff	1. Prescriber-only facilities: (a) Small group sessions in which guidelines were modified on the basis of prescriber feedback (b) Laminated pocket cards summarizing treatment of pneumonia 2. Prescriber and nursing staff facilities: (a) Small group sessions for providers and nursing staff (b) Laminated pocket cards summarizing treatment of pneumonia (c) Laminated posters placed near facility telephones used to contact prescribing providers	1. Guideline adherence (before/after): (a) All NHs: (i) All antibiotics: 60.1 vs 67.2 % (NS) (ii) PO antibiotics: 57.6 vs 59.6 % (NS) (iii) IV antibiotics: 62.2 vs 73.4 % ($P < 0.02$) (b) Provider-only education: (i) IV antibiotics: 64.5 vs 69 % (NS) (c) Provider and nursing staff education: (i) IV antibiotics: 50 vs 81.8 % ($P = 0.13$) 2. 30-day mortality (before/after): (a) All NHs: 23.9 vs 18.1 % (NS)
Loeb et al. [80]	Design: cluster-randomized study in 24 NHs Focus: UTI Randomization: 12 NHs allocated to a multifaceted intervention and 12 NHs allocated to usual care	1. Diagnostic and treatment algorithm for UTI 2. Education of nursing staff (small group) and prescribers (individual) 3. Pocket cards and posters with algorithms	1. Treatment of suspected UTI (intervention vs usual care): (a) Antibiotic starts: −0.49 per 1000 resident-days (95 % CI −0.93 to −0.06) (b) DDDs: −3.85 per 1000 resident-days (95 % CI −7.37 to −0.34) 2. Treatment of all infections (intervention vs usual care): (a) Antibiotic starts: −0.37 per 1000 resident-days (95 % CI −1.17 to 0.44)
Schwartz et al. [81]	Design: before/after, single-centre study Focus: all infections Randomization: N/A	1. Locally developed prescribing guideline 2. Audit of baseline rates of antibiotic resistance in the study facility 3. 4 small group sessions demonstrating case-based application of guidelines and review of resistance audit 4. Pocket booklet of prescribing guideline	1. Infection management (based on random sample of 100 pre- and 100 post-intervention cases): (a) Diagnostic accuracy: 32 vs 62 % ($P = 0.006$) (b) Treatment concordance with guidelines: 11 vs 39 % ($P < 0.001$) 2. Antibiotic utilization (all prescribing events): (a) Antibiotic starts: −25.9 % ($P = 0.06$) (b) Antibiotic days: −29.7 % ($P < 0.001$)
Monette et al. [89]	Design: cluster-randomized study in 8 NHs Focus: all infections Randomization: 4 NHs allocated to multifaceted intervention and 4 NHs allocated to usual care	1. Antibiotic guide mailed to prescribers; initial mailing followed by second mailing 4 months later 2. Individual profile of prescribing patterns (guideline adherence) over previous 3 months mailed to providers; initial mailing followed by second mailing 4 months later	1. Likelihood of guideline non-adherence in intervention arm: (a) After first mailing: 0.47 (95 % CI 0.21–1.05) (b) After second mailing: 0.36 (95 % CI 0.18–0.73) (c) 6-month follow-up: 0.48 (95 % CI 0.23–1.02)

Table 1 continued

References	Study characteristics	Interventions	Outcomes
Zabarsky et al. [82]	Design: before/after, single-centre study Focus: UTIs Randomization: N/A	1. Baseline and semi-annual education of nursing staff focused on indications for testing resident urine samples 2. Baseline and semi-annual education of primary care staff focused on diagnosis of UTI and avoiding treatment of ASB 3. Pocket reference cards tailored to nursing and primary care staff roles 4. Posters displayed at computer stations used by nursing and primary care staff 5. Audit and feedback to nursing and primary care staff when inappropriate testing and treatment of ASB identified	1. Urine culture rate (before/after): decreased from 3.7 to 1.5 cultures per 1000 resident-days (IRR 0.41; 95 % CI 0.27–0.64; $P < 0.001$) 2. ASB treatment rate (before/after): decreased from 1.7 to 0.6 events per 1000 resident-days (IRR 0.37; 95 % CI 0.19–0.72; $P = 0.002$) 3. Antibiotic days of treatment (before/after): decreased from 167.1 to 117.4 antibiotic days per 1000 resident-days ($P < 0.001$)
Pettersson et al. [83]	Design: cluster-randomized study in 58 NHs Focus: all infections (guideline intervention primarily focused on management of UTI in women) Randomization: 29 NHs allocated to multifaceted intervention (26 included in final analyses) and 29 NHs allocated to usual care (20 included in final analyses) Outcome data collected by participants rather than investigators	1. Regionally developed antibiotic prescribing guideline 2. Audit of baseline prescribing patterns and local antibiotic resistance patterns 3. 2 educational sessions delivered to nursing staff and prescribing providers, focused on: (a) Content of prescribing guideline (b) Review of facility-specific prescribing patterns and local antibiotic resistance patterns (c) Identification of barriers to change 4. Printed educational materials focused on hygiene and prescribing guideline disseminated	1. Primary outcome: (a) Change in percentage of female residents receiving a fluoroquinolone antibiotic for treatment of UTI: −0.196 in intervention NHs vs −0.224 in control NHs (diff-in-diff: 0.028; 95 % CI −0.193 to 0.249) 2. Secondary outcomes: (a) Change in percentage of residents receiving an antibiotic for treatment of any infection (before/after): −0.076 in intervention NHs and 0.048 in control NHs (diff-in-diff: −0.124; 95 % CI −0.228 to −0.019) (b) Change in percentage of residents managed with 'wait and see' approach (before/after): 0.093 in intervention NHs vs −0.051 in control NHs (diff-in-diff: 0.143; 95 % CI 0.047–0.240) (c) Change in percentage of residents receiving an antibiotic for UTI (before/after): −0.031 in intervention NHs vs −0.070 in control NHs (diff-in-diff: 0.038; 95 % CI −0.013 to 0.089)

Table 1 continued

References	Study characteristics	Interventions	Outcomes
Linnebur et al. [90]	Design: quasi-experimental study in 16 NHs Focus: NH-acquired pneumonia Randomization: 8 NHs in Colorado non-randomly allocated to a multifaceted intervention and 8 NHs in Kansas and Missouri serving as controls	1. Change tools: (a) Evidence-based pneumonia care pathway developed (b) Standardized order forms 2. Implementation strategies: (a) Brief educational session focused on guidelines and pneumonia pathway delivered to prescribing providers at baseline (b) Reinforcement phone calls 3 months after baseline education and in year 2 of the study (c) Paid nurse liaison in study NHs to champion use of pneumonia pathway and collect study data	1. Change in guideline adherence (before/after): +6 % in intervention NHs vs +7 % in control NHs ($P = 0.3$) 2. Change in delivery of antibiotic within 4 hours (before/after): +18 % in intervention NHs vs −7 % ($P < 0.001$)
Jump et al. [110]	Design: before/after, single-centre study Focus: all infections Randomization: N/A	1. Weekly infectious disease consultant review of residents receiving antibiotics, with feedback of recommendations to providers 2. 24/7 telephone infectious disease consultative services made available to prescribing providers	1. All antibiotic DOT (before/after): decreased from 175.1 to 122.3 days per 1000 resident-days (IRR 0.60; $P < 0.001$) 2. Oral antibiotic DOT (before/after): decreased from 136.1 to 93.1 days per 1000 resident-days (IRR 0.59; $P < 0.001$) 3. Intravenous antibiotic DOT (before/after): decreased from 39.0 to 29.3 days per 1000 resident-days (IRR 0.75; $P = 0.01$)
Frentzel et al. [84]	Design: quasi-experimental study in 12 NHs Focus: UTIs Randomization: 4 NHs allocated to the standardized form intervention using a high-intensity implementation plan, 4 NHs allocated to the standardized form intervention using a low-intensity implementation plan and 4 NHs allocated to usual care	1. Change tools: (a) Standardized form designed to structure documentation of resident signs/symptoms and facilitate decision-making around treatment of UTI 2. Implementation strategies: (a) Letter describing purpose of form sent out to providers (b) In-person training of nursing staff (1 session in low-intensity NHs and 2 sessions in high-intensity NHs) (c) Technical support for intervention NHs (passive in low-intensity NHs and active in high-intensity NHs)	1. Change in treatment of ASB: (a) High-fidelity NHs ($n = 4$; before/after): decreased from 73.2 to 49.4 % (regression-adjusted OR 0.35; 95 % CI 0.16–0.76) (b) Low-fidelity and control NHs ($n = 8$; before/after): decreased from 69.6 to 68.8 % (regression-adjusted OR 1.93; 95 % CI 1.05–3.56)

Table 1 continued

References	Study characteristics	Interventions	Outcomes
Zimmerman et al. [85]	Design: quasi-experimental study in 12 NHs Focus: respiratory infections and UTIs Randomization: 6 NHs in one geographic region allocated to multifaceted intervention and 6 NHs in another geographic region allocated to usual care	1. Standardization of inter-professional communication through MCRF 2. Nurse in-services focused on use of MCRF, as well as identification and testing of residents with suspected infection 3. Prescriber education focused on purpose of MCRF, as well as diagnosis and treatment of common infections 4. Pocket cards summarizing content of educational sessions 5. Resident/family informational brochure focused on benefits and risks of antibiotic therapy 6. Facility-level review of adherence to treatment recommendations addressed in educational sessions	1. All antibiotic starts per 1000 resident-days (before/after): −3.65 in intervention NHs and −0.90 in control NHs (diff-in-diff −2.75; regression-adjusted IRR 0.86; 95 % CI 0.79–0.95) 2. Antibiotic starts for respiratory tract infection: IRR 0.71 (95 % CI 0.56–0.90) 3. Antibiotic starts for UTI: IRR 0.84 (95 % CI 0.66–1.05) 4. Antibiotic starts for skin and soft tissue infection: IRR 0.89 (95 % CI 0.62–1.28)
Furuno et al. [91]	Design: before/after, single-centre study Focus: culture-confirmed infections Randomization: N/A	1. Facility-specific antibiograms (frequency tables summarizing rates of resistance to selected antibiotics among different types of bacteria) were developed 2. Results of antibiograms were presented at in-services with advice on how to use these data when selecting antibiotic therapy	1. Culture-concordant antibiotic therapy increased from 32 to 45 % ($P = 0.32$)
Fleet et al. [109]	Design: cluster-randomized study in 30 NHs Focus: all infections Randomization: 15 NHs allocated to a prescribing care bundle intervention and 15 NHs allocated to usual care	1. 'Initiation of Treatment' form focused on the following process elements: (a) Documentation of resident signs/symptoms (b) Documentation of diagnosis (c) Obtaining tests before starting antibiotic (d) Timing and appropriateness of antibiotic 2. 'Review of Treatment' form focused on the following process elements: (a) Review of resident progress (b) Review of test results (c) Stop date and outcomes of treatment documented	1. Antibiotic starts per 100 residents (before/after): +0.06 ($P = 0.94$) in intervention NHs vs +0.56 ($P = 0.4$) in control NHs 2. Antibiotic consumption (DDDs) per 1000 resident-days (before/after): −3.25 ($P = 0.02$) in intervention NHs vs +2.24 ($P = 0.04$) in control NHs

Table 1 continued

References	Study characteristics	Interventions	Outcomes
Doron et al. [86]	Design: before/after study in 17 NHs Focus: UTIs Randomization: N/A	1. Change tools: (a) UTI protocol to guide decisions about testing and treatment (b) Clinician educational curriculum focused on appropriate urine testing and avoidance of treating ASB (c) Resident/family member educational curriculum about UTI and risks and benefits of antibiotics (d) Posters and handouts summarizing important aspects of educational curriculum (e) Data collection instrument and instructional materials 2. Implementation strategies: (a) 2 full-day workshops focused on rationale for and use of change tools (b) Regular webinars focused on implementing change tools (c) Collaborative conference calls (d) One-on-one coaching	1. Urine culture rate: IRR 0.73 (95 % CI 0.66–0.79) 2. UTI treatment rate: IRR 0.67 (95 % CI 0.59–0.76) 3. *Clostridium difficile* rate: IRR 0.55 (95 % CI 0.39–0.78)
Trautner et al. [87]	Design: before/after study with contemporary control group Focus: UTIs Randomization: N/A	1. Algorithm created to make catheter-associated UTI and ASB guidelines applicable at point of care 2. Use of algorithm taught through case-based audit and feedback during in-services	1. Number of urine cultures ordered (acute and long-term care) decreased from 41.2 to 23.3 per 1000 bed-days during the intervention year ($P < 0.0001$) and decreased further during the maintenance year to 12.0 per 1000 bed-days ($P < 0.0001$) 2. Treatment of ASB decreased from 52 to 10 % ($P = 0.001$) in long-term care intervention units

ASB asymptomatic bacteriuria, *CI* confidence interval, *DDD* defined daily dose, *diff-in-diff* difference-in-differences, *DOT* days of therapy, *IRR* incidence rate ratio, *IV* intravenous, *MCRF* medical care referral form, *N/A* not applicable, *NH* nursing home, *NS* not significant, *OR* odds ratio, *PO* oral, *UTI* urinary tract infection prescribing for pneumonia in New York nursing homes demonstrated a significant improvement in adherence to prescribing guidelines (from 50 to 82 %) in facilities where education was targeted at both types of clinical staff [88]. In contrast, guideline adherence remained essentially unchanged (69 versus 65 %) in nursing homes where education was targeted solely at prescribing providers [88].

5.4 De-Escalation Interventions

Post-prescribing review and de-escalation interventions (Q3–5 in Fig. 1) have had a profound impact on antibiotic utilization in hospitals [106]. Not surprisingly, there is evidence that de-escalation interventions have the potential for similar impact in nursing homes. Fluoroquinolones are among the most commonly prescribed antibiotics in US nursing homes [14]; however, studies have shown that providers rarely switch to agents with a more narrow spectrum (e.g. trimethoprim–sulfamethoxazole) even when culture results indicate a fully susceptible pathogen [23]. Moreover, a large observational study of nursing homes in Ontario demonstrated that the majority of antibiotic prescriptions exceeded durations of therapy sufficient for treatment of the most commonly encountered infections [17]. A follow-up study by these investigators confirmed that only a minority of prescribers (22 %) employed short-course therapy accepted in most guidelines [107]. Convincing providers who typically prescribed antibiotics for longer durations to prescribe antibiotics in a similar manner would reduce the total number of antibiotic days in Canadian nursing homes by 17 % [107]. A recently published study of 100 prescribing events in a VA nursing home demonstrated that 43 % of 1351 antibiotic days associated with these events could have been safely eliminated either by stopping the antibiotic because it was unnecessary or by shortening the duration of therapy [108].

Despite these opportunities, antibiotic de-escalation interventions remain poorly studied in the nursing home setting. A cluster-randomized study of a multi-component intervention, which included a routine post-prescribing review of empirically initiated antibiotics in 30 nursing homes in London, demonstrated a 5 % reduction in antibiotic consumption in intervention facilities compared with control facilities despite low adherence to the post-review procedures (26 %) [109]. Another study examined the impact of an infectious disease consultative service, which involved remote consultation services during daytime hours, as well as once-weekly in-person resident assessments, on antibiotic prescribing and resident outcomes in a 160-bed VA nursing home [110]. Significant declines in systemic antibiotic use (-30 %; $P < 0.001$) and facility rates of *C. difficile* (slope -0.03; $P = 0.04$) were observed over the 18-month intervention period in this study.

6 Suggested Approach to Antibiotic Stewardship in Nursing Homes

While there are many barriers to be overcome, the available data do suggest that antibiotic prescribing patterns in nursing homes can be improved through interventions that target different phases of the antibiotic prescribing process (Fig. 1). Combining interventions that target the different phases of the prescribing process and mitigate against influences that promote inappropriate antibiotic prescribing decisions (Fig. 2) has intrinsic appeal [85] but requires more study [111]. These technical observations aside, sustainability of any particular intervention is unlikely unless nursing homes develop a dedicated focus on improvement (Fig. 2—facility and staff factors) [112]. With this in mind, we propose that nursing homes first develop structures and processes focused on understanding local patterns, determinants and outcomes of antibiotic use (Sects. 6.1–6.4), and then leverage this infrastructure to develop staff/provider education (Sect. 6.5) and implement targeted process interventions (Sect. 6.6).

6.1 Make Antibiotic Stewardship a Quality Improvement Focus

Changing nursing home culture requires commitment at an organizational level. Consequently, the first step is to obtain buy-in from the facility leadership, including the director of nursing and the medical director, to make antibiotic stewardship a facility quality improvement focus. Arguments that nursing home leaders find persuasive include (1) a need to satisfy regulatory requirements focused on appropriate use of medications; (2) federal mandates to demonstrate meaningful organizational quality assurance and performance improvement (QAPI) [113]; (3) emerging federal policies to promote and ultimately require antibiotic stewardship activities across all health care settings [6]; (4) organizational costs of treating antibiotic-resistant infections and CDI [25, 114]; and (5) how certain antibiotic stewardship interventions, particularly those focused around enhancing interdisciplinary communication, can generate corollary benefits in other nursing home processes and outcomes (e.g. enhanced management of resident changes in condition).

6.2 Assemble a Team

Antibiotic prescribing in nursing homes is a complex problem and involves a number of factors [115]. Facilities dedicated to improving the quality of antibiotic prescribing should assemble a multidisciplinary team that, at a minimum, involves the facility medical director, the director of nursing, an infection control practitioner and, if available, the facility pharmacist [116]. Initial meetings should focus on identification of outcome measures that will be targeted by improvement efforts, resources that will be needed to achieve these objectives, and duties and responsibilities of team members and expectations of nursing home staff and prescribing providers as they relate to antibiotic use in the facility. Seeking input from individuals with expertise in antibiotic stewardship and infectious diseases in the region can be particularly helpful at this stage. This team should plan to meet at least monthly when first getting started.

6.3 Develop and Implement Basic Policies, Guidelines and Goals

Provider orders for antibiotics should include clear documentation of the drug, dose, duration and indication. This latter requirement is critical for tracking antibiotic utilization (see below). Policies should be developed that discourage the use of prophylactic antibiotics for prevention of UTI and routine urine dipstick testing when evaluating a resident experiencing a change in condition. The antibiotic stewardship team should also consider developing policies and guidelines that limit the use of fluoroquinolone antibiotics, given their strong relationship to *C. difficile* [117] and high rates of resistance among urinary pathogens in many facilities [91, 118, 119]. More detailed guidelines that specify the choice and duration of antibiotic therapy for commonly encountered syndromes can be very effective in improving prescribing quality [81] but may require substantial effort to develop.

6.4 Measure and Report Outcomes and Key Process Indicators

A capability to measure and track process and outcomes is a fundamental characteristic of successful quality improvement [120]. Most nursing homes routinely track commonly encountered infections [52, 121]. Adapting this process to monitor, at a minimum, UTI events and CDI should not prove too difficult for most facilities. We recommend that UTI be tracked in two ways: (1) treated UTI events (i.e. all antibiotic starts regardless of whether the event was a true infection); and (2) surveillance-defined UTI events (i.e. only those events that satisfy published criteria) [121, 122]. These measures can then be tracked in a number of ways. Point prevalence measurements (e.g. measuring the numbers of UTI events in the months before and after an intervention) are relatively easy to perform. Tracking outcomes using rates (e.g. UTI events per month/resident-days per month $\times$ 1000) is a more rigorous approach, which may allow a facility to more accurately assess the impact of multiple interventions over time. CDI can be tracked in a similar manner using the National Healthcare Surveillance Network (NHSN) criteria, which consider the rate of non-duplicative positive tests per 10,000 resident-days [123]. Nursing homes may also consider including residents transferred to their facility with *C. difficile* in that rate [124]. Extending monitoring to other types of infections, including those involving the respiratory tract and soft tissues, should be considered, as these are the second and third most common indications for initiation of antibiotic therapy in the nursing home setting [14, 125]. Finally, facilities should discuss developing a facility-specific antibiogram [119] in consultation with their contract laboratory. The antibiogram is a tool that facilities can use to identify common resistance patterns (e.g. high levels of fluoroquinolone resistance), which may influence providers' empirical antibiotic decisions [91]. The small number of cultures collected in nursing homes may create instability in observed patterns of resistance and should be interpreted in consultation with individuals with infectious disease expertise.

Nursing homes embarking on quality improvement in antibiotic prescribing should seek to track antibiotic use in some manner. Logistics, as well as the types of improvement interventions that will be pursued, should guide the measure(s) selected. Most nursing homes employ tracking methods to identify residents experiencing a change in condition, including those residents who are currently receiving antibiotics [126]. Consequently, information on antibiotic starts is readily available and can be tracked at predefined time periods by the individual responsible for infection surveillance in the facility. Cross-sectional assessments of antibiotic use involve counting the number of resident on antibiotics during a given day or week. These assessments are fairly simple and do not require a huge amount of effort, but they may not be as sensitive to change as measures that are tracked more regularly. Tracking antibiotic starts per month (like other continuously monitored outcomes, this measure should be converted to a rate using resident-days as a denominator) is a more involved process, which allows facilities to trend and visualize their data. These data can be further stratified by indication (antibiotic starts for UTI, respiratory tract infection, skin and soft tissue infection), particularly if the indications for the antibiotic are routinely included on prescriber orders (see above). Antibiotic start data are ideal for tracking the effects of interventions focused on reducing unnecessary antibiotic use (e.g. reducing urine cultures) but may not be very informative for interventions that focus on reducing the duration of antibiotic therapy (e.g. guidelines or de-escalation). Facilities seeking to implement interventions along these lines should seek to track antibiotic utilization using either a days of therapy (DOT) measure [127] or a defined daily dose (DDD) measure [16]. The DOT utilization measure is derived by adding up every

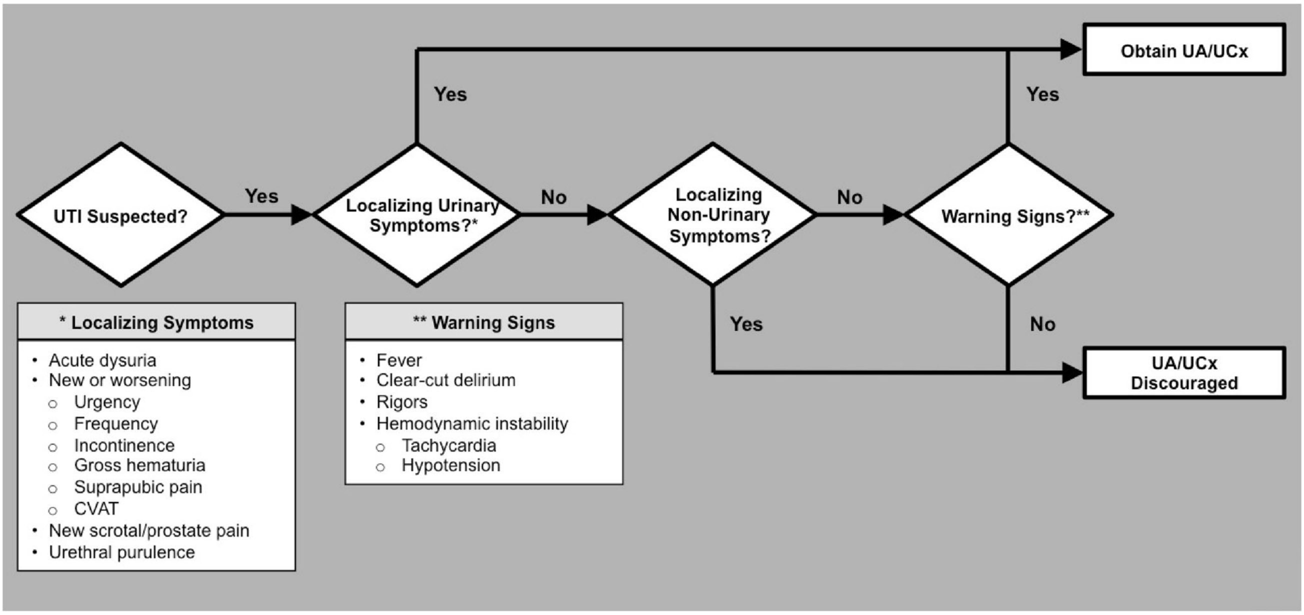

Fig. 3 Decision pathway to reduce unnecessary diagnostic testing of urine samples in long-term care facilities (adapted from Crnich and Drinka [94]). *CVAT* costovertebral angle tenderness, *UA* urinalysis, *UCx* urine culture, *UTI* urinary tract infection

day on which a resident receives a unique antibiotic. By this method, receipt of multiple antibiotics has additive effects on the measure (e.g. a resident who receives 5 days of ceftriaxone and 5 days of azithromycin would generate 10 DOT even if both antibiotics are administered on the same day). In contrast, the DDD utilization measure is based on overall consumption of a particular antibiotic adjusted for typical daily dosing in an adult patient with intact renal function. By this approach, the total number of grams of each antibiotic used (or purchased) are summed over the period of interest and divided by the World Health Organization's assigned DDD value [128]. Manual collection of these types of data poses a challenge. Consequently, working with the facility pharmacist to automate this process through queries of the pharmacy information system is recommended.

6.5 Education

Education is a foundational activity of any ASP and can be used to target all three domains influencing prescribing decisions in nursing homes (Fig. 2—patient and family factors, facility and staff factors, health care provider factors). Educational content should cover the importance of stewardship, plans for implementation of specific stewardship activities and the responsibilities of clinical staff in achieving stewardship goals. Education should be targeted and tailored to nursing assistants, nursing staff, providers, residents and families. While not focused on antibiotic prescribing practices, a recently published study performed in 12 Michigan nursing homes demonstrated that a multimodal educational intervention focused on common infection prevention practices and care processes associated with indwelling urinary catheters and feeding tubes was associated with significant reductions in rates of MRSA acquisition [absolute risk reduction (ARR) 0.78; 95 % CI 0.65–0.95] and catheter-associated UTI (ARR 0.69; 95 % CI 0.49–0.99) [129]. Resident and family education, when combined with staff and provider education, as well as interventions to enhance interdisciplinary communication, has also recently been shown to be associated with reductions in antibiotic use in nursing homes [85]. Studies such as these demonstrate that educational interventions can be powerful tools for changing behaviours but likely need to target multiple individuals [88] and be delivered via a number of modalities—including in-service training sessions, newsletters, pocket guides, posters and brochures—in order to be maximally effective.

6.6 Next Steps

Once a facility has established its basic policies, outcome and process measures and has developed basic educational activities, the stewardship team should use the collected data to set new goals and select more active strategies in order to achieve these goals. As noted above, antibiotic decision-making in nursing homes is heavily influenced by diagnostic test results, and we believe that facilities will see the biggest return on investment through a focus on implementing interventions to reduce orders for urine cultures. Urine dipstick and urinalysis tests, despite being reliable methods for ruling out bacteriuria [130, 131], are often used to justify orders for urine cultures. Mild abnormalities on urinalysis, such as positive nitrite or leukocyte esterase readings on dipsticks, or moderate numbers of white blood cells on microscopy, are common in asymptomatic bacteriuria [96, 97], so neither test should be used as a screen for UTI. Consequently, nursing homes should instead develop and use protocols that restrict all urine testing to residents with a high probability of having a UTI (Fig. 3). These protocols should be operationalized not only through education of providers but, given their influence on provider decision-making [42, 43], also through engagement of nursing staff, who should be empowered to discourage providers from ordering diagnostic urine tests in the absence of specific evidence-based criteria. Tracking the frequency of urine cultures and the number of treated UTI events that do not satisfy surveillance definitions [121] provides targets that a facility can follow in order to assess the impact of the intervention. Other approaches based on improving interdisciplinary communication through tools that standardize documentation and sharing of important patient information, as well as development of a process to ensure consistent post-prescribing review and de-escalation, may represent a greater challenge but are worth considering, particularly if success in reducing the frequency of urine cultures has been achieved.

7 Unanswered Questions and Future Directions

The emerging crisis in antibiotic resistance will require a concerted effort to improve antibiotic stewardship across all health care settings [6]. Considerable progress has been made in our understanding of the extent and determinants of inappropriate antibiotic use in nursing homes. While there is accumulating evidence that interventions focused on processes (e.g. urine testing) associated with the initial antibiotic decision can reduce unnecessary antibiotic use, there remains a critical need to identify interventions that target post-prescribing decision-making (e.g. review and de-escalation). There is also a need for more research on how to implement both types of stewardship interventions with fidelity and sustain them over time, particularly in nursing homes with limited quality improvement resources. Finally, there is a need for studies that evaluate the effects of stewardship interventions on facility and resident outcomes, including health care costs, as well as rates of infections caused by *C. difficile* and multidrug-resistant bacteria.

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