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Reliability of nonlocalizing signs and symptoms as indicators of the presence of infection in nursing-home residents

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Antibiotics are among the most common medications prescribed in nursing homes. The annual prevalence of antibiotic use in residents of nursing homes ranges from 47% to 79%,[1] and more than half of antibiotic courses initiated in nursing-home settings are unnecessary or prescribed inappropriately (wrong drug, dose, or duration).[2-8] Inappropriate antibiotic use is associated with a variety of negative consequences including *Clostridioides difficile* infection (CDI),[2] adverse drug effects,[9-11] drug–drug interactions, and antimicrobial resistance.[12-14] In response to this problem, public health authorities have called for efforts to improve the quality of antibiotic prescribing in nursing homes.[15-17]

There is increasing interest in implementing interventions to promote the deliberate application of clinical criteria as an approach to improving antibiotic decision making in nursing homes.[18-20] A consensus conference held by members of the Society for Healthcare Epidemiology of America (SHEA) first developed minimum criteria that should be present before prescribing antibiotics in long-term care settings,[7] known as the "Loeb Minimum Criteria."[7] These criteria were developed with clinicians' empiric antibiotic decision-making in mind; they contrast with existing infection surveillance criteria that were designed primarily for the retrospective determination of treatment appropriateness from of laboratory and imaging study results.[21] The Loeb Minimum Criteria, published in 2001, have allowed practitioners to make decisions regarding whether to start antibiotics for a resident before laboratory and imaging results are available.[7]

Since then structure and delivery of nursing home care has changed significantly.[7] For this reason, SHEA convened an expert panel to examine nonlocalizing signs and symptoms as indicators of infection in residents of nursing homes, such as behavior changes and falls, which practitioners may consider indicators of infection and reasons to initiate antibiotics. For example, in a prospective cohort study of residents of 25 nursing homes, the most documented presenting symptom for suspected urinary tract infection (UTI) was mental status changes.[22] In a survey of nursing-home practitioners, the most common triggers for suspecting UTIs in residents of nursing homes were changes in mental status (93%) and fever (83%).[23]

Practitioners may base empiric antibiotic prescribing decisions for nursing-home residents with nonlocalizing signs or symptoms on the premise that manifestations of infection change with age and that older adults with infections present differently than younger adults.[24,25] For example, fever—a cardinal sign of infection—can be blunted or absent in older adults with serious bacterial infections.[26] Likewise, dementia can present significant challenges to diagnosis, including difficulty in obtaining a reliable history. Although individual studies may point to an association of a nonlocalizing symptom with infection, within the body of literature, the reliability of nonlocalizing signs and symptoms in establishing a clinical suspicion of infection remains poorly understood.

The misattribution of nonlocalizing signs and symptoms to infection represents a major barrier to improving the appropriateness of antibiotics in nursing homes. Thus, we evaluated the clinical reliability of several nonlocalizing signs and symptoms as indicators of infection among residents of nursing homes, and our results and recommendations are presented here. This guidance document is intended to form the foundation for an update to the Loeb Minimum Criteria,[7] and it will be followed by another

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document addressing evaluation for specific syndromes and use of antibiotics to treat them.

Intended use

This document outlines the relationship between nonlocalizing signs and symptoms as a manifestation of an infection in residents of facilities that provide skilled (postacute) nursing services and residential care to adults. It is intended to form the foundation for an update to the Loeb Minimum Criteria[7] and to guide clinicians in evaluating signs and symptoms that commonly contribute to inappropriate antibiotic use. It is also intended to assist clinicians with evaluation of whether nonlocalizing signs or symptoms are sufficiently reliable to justify initiation of antibiotics.

We have emphasized specific patient populations, including residents with advanced dementia, because formal surveillance definitions of infections in long-term care settings do not exist.[27] The primary purpose of the work was to determine the extent to which specific nonlocalizing signs and symptoms, when they are present in isolation, should elevate clinical suspicion of infection, if at all. In a forthcoming document under development, we will address the extent to which nonlocalizing findings contribute to establishing a clinical suspicion of infection when present in combination with other focal and nonfocal findings.

The scope of this guidance includes nursing-home residents, most of whom are older adults. In 2014, ~15% of nursing-home residents were aged <65 years.[28] This guidance document does not distinguish between younger and older adult nursing-home residents. Furthermore, the scope of the guidance does not include residents of long-term acute-care hospitals (LTACHs), geriatric psychiatric units, or assisted living facilities, though these recommendations may be applicable to residents of geriatric psychiatric units or assisted-living facilities. This document does not address the treatment of pediatric nursing-home residents or those institutionalized primarily for psychiatric disease.

This guidance is intended to reflect an assessment of the strength of association between bacterial infections and geriatric manifestations and should not be used as the basis for excluding a diagnosis of respiratory viral pathogens such as SARS-CoV-2, influenza, or respiratory syncytial virus (RSV).

SHEA develops special-topic expert guidance documents with relatively narrow scope that lack the level of evidence required for a formal guideline developed using "Grading of Recommendations Assessment, Development and Evaluation" (GRADE) or a similar systematic methodology, but are important in providing safe, effective healthcare.[29] As such, the systematic grading of the evidence level is not provided for the individual recommendations. Each expert guidance document is based on a synthesis of evidence, theoretical rationale, current practices, practical considerations, writing group opinion, and consideration of potential harm, where applicable. Within the document, a summary list of expert guidance recommendations is provided along with the relevant rationale.

This expert guidance was developed following the process outlined in the *Handbook for SHEA-Sponsored Guidelines and Expert Guidance Documents*.[30] No guideline or expert guidance document can anticipate all clinical situations, and this guidance document is not meant to be a substitute for individual clinical judgment by qualified professionals.

Authors

The authors of this guidance include current and past members of the Society for Healthcare Epidemiology of America (SHEA) Guidelines Committee (GLC) and the SHEA Long-Term Care Special Interest Group. Dr Robin Jump served as an author and the representative for the Society of Post-Acute and Long-Term Care (AMDA), Dr Sarah Doernberg served as an author and the representative for the Infectious Diseases Society of America (IDSA), and Dr Andrew Morris served as an author and the representative for the Association of Medical Microbiology and Infectious Disease Canada (AMMI Canada). All authors served in a voluntary capacity.

Methods

In 2016, members of the SHEA Long-Term Care Special Interest Group with expertise in infections in residents in nursing home settings agreed to develop a document to systematically evaluate the association between infection and a number of nonlocalizing signs and symptoms commonly encountered in nursing-home residents. The topic of "the initiation of antibiotics in long-term care settings" was among those proposed and selected by the SHEA Guidelines Committee (GLC). The subsequent manuscript proposal developed by the GLC was approved by the SHEA Publications Committee and the Board of Trustees.

We identified themes and, based on these, developed "population, intervention, control, and outcomes" (PICO)-style questions for expert guidance. These questions were used in the development of search terms (medical subject heading [MeSH] and text word), and both the questions and search terms were discussed and voted upon until unanimous approval was achieved. We identified articles published between January 1, 1990, and June 20, 2018. Only English-language articles were included. The lists of articles generated from the search were reviewed by a primary reviewer and secondary reviewer for inclusion and were adjudicated by the chair (C.C.) and vice chair (T.R.) if needed.

This document provides a summary of expert guidance recommendations along with relevant rationale.

SHEA expert guidance documents are developed with a formalized process for reaching expert consensus. Recommendations are listed with rationale statements that take into account relevant evidence as well as the consensus of the group. Consensus around recommendations and rationale were determined using an anonymous ranking and comment period. Recommendations and rationale statements that did not receive unanimous agreement were discussed. Full consensus was achieved. The document was reviewed by the SHEA Guidelines Committee, SHEA Antimicrobial Stewardship Committee, and SHEA Board of Trustees, the Society for Post-Acute and Long-Term Care Medicine (AMDA), the Association of Medical Microbiology and Infectious Disease Canada (AMMI Canada), the Infectious Diseases Society of America (IDSA), the National Association of Directors of Nursing Administration in Long Term Care (NADONA), and the Society of Infectious Diseases Pharmacists (SIDP), and was endorsed by SHEA, AMDA, AMMI Canada, IDSA, and SIDP.

Guidance statement

Note: Appendix 1 *(online) provides a table summarizing the nonlocalizing symptoms that should and should not prompt further evaluation for infection, as well, where applicable based on the*

published literature, potential noninfectious causes of the signs and symptoms and suggested next steps.

Evaluation for infection in nursing-home residents

Older adults may manifest acute illness with atypical signs and symptoms, including those that are nonlocalizing; however, most nursing-home residents with an acute infection also will exhibit some localizing signs and symptoms of infection. Within this manuscript, we have noted several isolated, nonlocalizing signs and symptoms that should raise suspicion for the presence of infection. In these situations, clinicians should consider noninfectious explanations for the nonlocalizing sign or symptom before embarking on an evaluation for infection. Changes to medication, dehydration, undertreated pain, constipation, sleep deprivation, and misuse of assistive devices are common triggers of behavioral change in nursing residents with cognitive impairments.

A period of careful active monitoring, during which vital signs and nursing staff assessments are performed more frequently and the affected resident is encouraged to take oral hydration and appropriate analgesia, can be an effective in avoiding unnecessary testing and treatment of the resident.[31] For residents who improve with these steps, no further evaluation for infection is needed. For residents who fail to improve or who manifest additional localizing signs or symptoms, active monitoring allows for early detection and initiation of targeted testing and treatment.

When an evaluation for infection is pursued, localizing signs and symptoms (eg, cough, shortness of breath), when present, should inform the assessment of nursing-home residents and indicate which diagnostic tests should or should not be ordered. It is important that clinicians not perform evaluations for infections at other sites (eg, urine). Use of a "panculture" approach to the evaluation of a suspected infection often leads to the detection of asymptomatic bacteriuria, which frequently leads to unnecessary antibiotic treatment.[32]

Symptoms that should prompt further evaluation for infection

Fever

What criteria should clinicians use to identify the presence of fever in a nursing home resident? **Recommendation:** We recommend that the criteria set forth in the "Clinical Practice Guideline for the Evaluation of Fever and Infection in Older Adult Residents of Long-Term Care Facilities: 2008 Update of the Infectious Disease Society of America"[25] be used to establish the presence of fever in a resident of a nursing home. These criteria include any of the following:

- A single temperature of >100°F (>37.8°C) or
- Repeated temperatures of >99°F (>37.2°C) or
- An increase in temperature of >2°F (>1.1°C) over the resident's baseline non-illness temperature.

Rationale: Many of the studies examining the temperature response in older adults with suspected infection do not employ consistent definitions of infection or employ diagnostic studies of dubious reliability,[33-35] making it difficult to establish the absolute operating characteristics of fever in this population. Nevertheless, ample evidence exists that basal temperatures in older adults are lower than those traditionally accepted as normal in younger adults (98.6°F or 37°C) and that diurnal variation in the temperatures of older adults are blunted.[36] For example, a

prospective observational cohort study documented that the mean baseline temperature of 50 nursing-home residents was >1°F below the commonly accepted standard baseline temperature (97.4°F or 36.3°C).[37] In another study, morning temperatures in 167 older adults and 21 high-school–aged students were similar but diverged significantly when temperature measurements were repeated in the afternoon.[36]

Based on review of these and other studies,[38-40] it is justifiable to employ a lower temperature threshold for establishing the presence of fever in older adults. In one early study, a temperature threshold of 101°F (38.3°C) had a sensitivity of only 40% for predicting infection in older residents of nursing homes.[39] Lowering the temperature threshold to 100°F (37.8°C) increased the sensitivity of detection of infection to 70%, while maintaining a high degree of specificity of 98.3%. In this study, reducing the temperature threshold to 99°F (37.2°C) reduced the specificity 89.9%, but documenting serial temperatures above this threshold may improve specificity.[41] There is insufficient evidence to indicate a specific time frame when evaluating for repeated temperatures of >99°F (>37.2°C). We suggest that 2 or more temperatures >99°F (>37.2°C) within a 24 to 48-hour period represent a fever. A temperature elevation of >2°F or >1.1°C above baseline values, while associated with some practical considerations, may be the most accurate method for establishing the presence of fever in older adults.[37,39,41]

The literature search we conducted did not identify studies to support a preferential recommendation for one temperature measurement method over others in the nursing-home setting. Although most of the studies of fever conducted in the nursing-home setting relied upon oral temperature measurement methods, tympanic-membrane and temporal-artery thermometers are increasingly utilized. Several studies have shown reasonably good correlation between methods that measure temperature at tympanic membrane and rectal locations.[39,42] Differences always exist in the absolute temperature measured at different body locations, and we recommend that serial temperature measurements on the same resident be conducted using the same method to avoid introduction of error from testing variation.

Should identification of fever in a nursing home resident prompt further evaluation for infection? **Recommendation:** Clinicians should perform further evaluation for infection in residents who meet 1 or more of the definitions of fever provided in the previous section, while considering the possibility of noninfectious causes of fever.

Rationale: It is important to consider noninfectious causes of fever in older adults, particularly if the history and exam do not reveal an obvious source of infection. Thermoregulatory capacity decreases with aging,[43] and older adults may be more likely to exhibit elevated temperatures when exposed to high environmental temperatures. Additionally, older adults are more likely to be prescribed medication that may trigger a febrile episode (eg, selective serotonin reuptake inhibitors). Nevertheless, the association between high-grade (≥102°F or 39.9°C) fevers and serious infection (eg, bacteremia) has been well documented,[44,45] and mortality is higher among nursing-home residents who exhibit altered body temperature as part of their infectious presentation.[46] We recommended that clinicians perform an infection work-up when they encounter fever in their nursing-home residents.

In accordance with existing guidelines,[25] we recommend that clinicians avoid indiscriminate diagnostic testing during the work-ups of a nursing-home residents with fever. A broader

diagnostic evaluation may be justified in those residents with isolated fever, particularly in those with advanced dementia who may have limited capacity to endorse localizing symptoms.[22]

Hypothermia

What criteria should clinicians use to identify the presence of hypothermia in a resident of a nursing home? **Recommendation:** We recommend that clinicians use the following temperature thresholds to define the presence of hypothermia:

- Two or more temperature measurements ≤95.9°F (≤36.0°C)[47] or
- Two or more temperature measurements documenting a decrease in temperature of >2°F (>1.1°C) from the resident's baseline non-illness temperature.

Rationale: Our literature search did not identify studies that could be used to establish temperature thresholds for the presence of hypothermia in residents of nursing homes. Due to the lack of published literature on the definition of hypothermia in older nursing-home residents, we generalized our search to include all adults. Consequently, we recommend that clinicians utilize the temperature criteria in the existing systemic inflammatory response syndrome (SIRS) definitions.[48,49] Older adults residing in nursing homes can often exhibit low baseline temperatures, as mentioned in the previous section, a study of 50 nursing-home residents found that baseline temperature averaged 97.4°F (36.3°C).[37] Accordingly, clinicians should consider negative deviations from baseline temperature of >2°F (>1.1°C) as an additional threshold for establishing the presence of hypothermia, particularly in residents whose baseline temperatures are near existing SIRS thresholds. Further, there is insufficient evidence to indicate a specific time when evaluating for repeated temperature measurements to assess hypothermia. We recommend that 2 or more temperatures of ≤95.9°F (≤36.0°C) or >2°F (>1.1°C) from the resident's baseline nonillness temperature indicate hypothermia. Both the temperature threshold for hypothermia and the time over which to assess serial temperature measurements require further study.

We recommend that clinicians confirm the presence of hypothermia detected by one method (eg, tympanic membrane) through measurement of either an oral or rectal temperature, and then use the same method to measure temperature to identify changes from baseline resident temperature. As noted, insufficient evidence exists to support a preferential recommendation for one temperature measurement method over another.

Should identification of new-onset hypothermia in a nursing home resident prompt further evaluation for infection? **Recommendation:** We recommend that clinicians further evaluate a resident who meets these definitions of hypothermia for the presence of infection, while considering the possibility of noninfectious causes of hypothermia.

Rationale: The diminishing thermoregulatory capacity associated with aging renders older adults more susceptible to hypothermia when exposed to low environmental temperatures. In addition, a number of health conditions, both chronic (eg, diabetes and hypothyroidism) and acute (eg, head injury and drug ingestions), may also manifest with hypothermia.

The literature search conducted for this manuscript did not identify studies focused on the relationship between hypothermia and infection in residents of nursing homes. However, studies that focused on the relationship between hypothermia and infection in older adults admitted to the hospital, some of whom may have been admitted from the long-term care setting, have shown that infection is a common cause of hypothermia.

Hypothermia is a well-described problem in older adults.[50] Although hypothermia is itself an uncommon presentation, infection, particularly sepsis, is one of the most commonly identified triggers identified in studies performed in hospitalized patients.[50-54] Consequently, we recommend that clinicians consider infection as a potential cause of hypothermia and that a diagnostic evaluation be performed to identify the cause.

Hypotension

What criteria should clinicians use to identify the presence of hypotension in a resident of a nursing home? **Recommendation:** We recommend that clinicians define hypotension as a systolic blood pressure of ≤90 mmHg in an individual with a previously normal systolic blood pressure.

Rationale: A reduced systolic blood pressure at the time of hospital admission is an independent predictor of mortality among nursing-home residents.[40] Although our literature search did not identify studies on the diagnostic accuracy of criteria to determine acute hypotension in residents of nursing homes, hypotension is commonly defined as follows:

- Systolic blood pressure of <90 mmHg or <100 mmHg or
- Decrease in systolic blood pressure of 40 mmHg or 50% from baseline or
- Mean arterial pressure or <60, <65, or <70 mmHg.[55]

We extensively discussed whether to recommend a systolic blood pressure threshold of ≤90 or ≤100 mmHg. Variation among guidelines' recommended blood pressure targets,[56-58] as well as concerns about the clinical benefits and side effects of antihypertensive therapy on physical and cognitive function[59] contribute to disparities in the baseline systolic blood pressures used in the nursing-home setting. In patients with bacteremia, both a systolic blood pressure of <90 mmHg[60] and <100 mmHg[61] have been associated with higher mortality. Although a systolic blood pressure of <100 mmHg, in combination with other physiological abnormalities, has been advocated as a threshold for early detection of sepsis in the nursing-home setting,[62,63] the published literature does not identify the operating characteristics of this blood pressure threshold, in isolation, as a factor in determining the presence of infection. Given that nearly a one-third of nursing residents have baseline systolic blood pressures below 120 mmHg,[64] as well as the high prevalence of orthostatic hypotension in this population,[65] we concluded that a systolic blood pressure threshold of ≤90 mmHg provides an appropriate balance between sensitivity and specificity among residents with baseline systolic blood pressures in the normal range. A systolic blood pressure threshold of ≤100 mmHg may be more appropriate in residents with a baseline systolic blood pressure >140 mmHg and would remain consistent with other guidelines designed for early detection of sepsis.[48,62]

Should identification of new-onset hypotension in a nursing home resident prompt further evaluation for infection? **Recommendation:** We recommend that clinicians further evaluate a resident who meets the definition of new-onset hypotension for the presence of infection while considering the possibility of noninfectious causes of hypotension.

Rationale: Sufficient evidence exists to link some episodes of hypotension to the presence of infection, although it is unclear whether definitions of hypotension based on absolute

measurements accurately predict shock and risk for mortality in residents of nursing homes. Several studies associate low blood pressure with poor outcomes when a patient is diagnosed with infection.[60,61] Postprandial and medication-induced orthostatic hypotension are common in residents of nursing homes and should not automatically trigger an evaluation for infection.[66,67] Consequently, we recommend that clinicians consider infection as a potential cause of new-onset hypotension and that they perform diagnostic evaluation to identify the cause of the hypotension.

Hyperglycemia

What criteria should clinicians use to identify the presence of hyperglycemia in a resident of a nursing home? **No recommendation.**

Rationale: Although well-described thresholds exist for when clinicians should consider treatment for underlying diabetes[68] and intensify therapy to reduce the risk of hyperglycemia-related complications, there are no well-established thresholds of hyperglycemia that should trigger a concern for infection in diabetic nursing-home residents. Consequently, we recommend that clinicians take an individualized approach when they identify new-onset hyperglycemia in a nursing-home resident that takes into account the individual's existing medication regimen, recent dietary patterns, and baseline pattern of glycemic control to determine whether the hyperglycemia is abnormal for that individual.

Should identification of new-onset hyperglycemia in a nursing home resident prompt further evaluation for the presence of infection? **Recommendation:** We recommend that clinicians further evaluate a resident with new-onset hyperglycemia for infection while considering the possibility of noninfectious causes of hyperglycemia.

Rationale: A well-known relationship exists between physiological stress and hyperglycemia in patients with known diabetes, as well as critically ill patients with relative underlying insulin resistance.[69] Infection often places nursing-home residents under physiological stress, which has been shown to affect glycemic control in those residents with diabetes[69]; however, our literature search did not identify studies that could establish how frequently an underlying infection triggers new-onset hyperglycemia in nursing-home residents with a diagnosis of diabetes. Given the paucity of literature on the subject, we emphasize the need for further research to identify the role of infection in new-onset hyperglycemia in nursing-home residents. We recommend that clinicians consider further evaluation for infection when treating nursing-home residents with new-onset hyperglycemia not otherwise explained by changes in medications, diet, or other conditions that may trigger acute physiological stress.

Delirium

What criteria should clinicians use to identify the presence of delirium in a resident of a nursing home? **Recommendation:** We recommend that clinicians use the Confusion Assessment Method (CAM) to identify the presence of delirium in a resident of a nursing home.[70] CAM requires the following:

- The presence of acute change in mental status with fluctuating discourse and
- Inattention and either of the following:
- Disorganized thinking or
- Altered level of consciousness.

Rationale: Guidelines for the evaluation of fever in nursing homes[25] and original nursing-home surveillance criteria[71] note that "worsening mental status" can be a nonspecific manifestation of acute infection in older nursing-home residents. However, many of the studies that formed the basis for this statement and similarly worded statements employed subjective clinician opinion rather than a reproducible measure of mental status change,[27] which undermines confidence in the strength of this relationship. This has propagated widespread belief that any change in mental status, no matter how minor (eg, increased irritability), may be an indication of underlying infection and has contributed to the problem of antibiotic overuse in nursing homes.[31,72,73]

The CAM has been shown to be sensitive (94%–100%) and specific (90%–95%) compared to the clinical diagnosis of delirium made by a psychiatrist.[70] In addition, the Nursing Home CAM (NH-CAM) can be used retrospectively to identify delirium based on the presence of diagnostic features recorded within the Minimum Data Set (MDS), a structured assessment instrument used on a regular basis to track clinical progress and resource utilization for nursing-home residents. Updates to surveillance definitions on infections in long-term care facilities[13] have moved away from subjective measures of mental status change and now employ the CAM tool in the list of constitutional criteria used to establish the presence of an infection. A recent study performed in Australian nursing homes demonstrated that the CAM tool can be used successfully to prospectively and retrospectively identify urinary tract infections.[74] Although the CAM currently serves as the most reliable method for detecting delirium, additional work may be needed to ensure that frontline staff members are able to reliably and accurately assess the individual elements of this instrument.[23]

Should identification of delirium in a nursing home resident prompt further evaluation for the presence of infection? **Recommendation:** We recommend that clinicians evaluate a resident who meets the definition of delirium for the presence of infection, while considering the possibility of noninfectious causes of delirium.

Rationale: Delirium in the frail and older nursing-home resident is a condition strongly associated with underlying dementia that may be precipitated by a number of infectious and noninfectious conditions, including medications and metabolic disorders.[75] Data supporting an association between delirium and an underlying infection in nursing-home residents are limited, and existing studies exhibit a number of methodological flaws.

Bookvar et al[76] evaluated residents at 3 nursing homes. Delirium was assessed using the CAM, but infections were diagnosed without additional criteria and clinicians commonly confused asymptomatic bacteriuria with urinary tract infection (UTI). Another report used chart review to identify delirium among patients. These researchers reported an association between delirium and a diagnosis of *C. difficile* infection, but they did not specifically evaluate whether new onset of delirium was a reliable indicator of underlying infection.[77] One systematic review of studies examining the association between delirium and UTI, performed among primarily noninstitutionalized older adults, did find a 2-fold higher prevalence of delirium subjects with UTIs compared to subjects without infection.[78] However, like studies performed in the nursing home setting, the studies included in this review suffered from methodological flaws. These limitations aside, residents who develop delirium have higher risk of loss of functional status, hospitalization, and death.[76,79,80] We recommend

that clinicians perform further evaluation for infection in those residents exhibiting delirium, particularly if another trigger for delirium cannot readily be identified.

Symptoms that should not prompt further evaluation for infection

Behavioral changes exclusive of delirium
Should identification of new-onset behavioral change(s), exclusive of delirium, in a nursing home resident prompt further evaluation for the presence of infection? **Recommendation:** We recommend that clinicians perform a formal delirium assessment when a behavioral change is newly identified in a nursing-home resident. If delirium has been excluded, we do not recommend further evaluation for infection unless additional, more specific signs and symptoms are present.

Rationale: Behavioral or psychiatric symptoms are among the most common triggers for suspicion of infection in residents of nursing homes[22,23]; however, limited information exists with regard to how these symptoms should be defined and whether they can be identified in a reproducible manner. Boockvar et al[81] developed a 5-item instrument to be used by nursing assistants to identify behavioral and/or psychiatric changes among residents. Although abnormal behaviors identified through use of the instrument positively correlated with subsequent development of an acute illness (either infectious or noninfectious), it showed a low level of consistency between staff using the instrument on different shifts of the same day ($\kappa = 0.16$; 95% confidence interval [CI], 0.03–0.28). Tingström et al[82] developed a 13-item instrument to be used by nursing assistants to facilitate the early identification of infection in long-term care residents. The instrument was developed through an iterative qualitative process with nursing assistants working in 2 long-term care facilities in Sweden[83] and prospectively evaluated in 6 long-term care facilities, also in Sweden. In this latter study, behavioral and/or psychiatric symptoms (eg, discomfort, pain, infirmity, and unrestrained, aggressive, or restless behaviors) were correlated with one another but exhibited a low correlation with focal or general symptoms (eg, fevers or rigors) indicative of an acute illness.[82] Data on interrater reliability were not reported in this study.

Both researchers and clinicians commonly consider change in behavior in the long-term care and nursing-home population a reliable indicator of acute illness, and particularly of infection, although the data supporting this claim are lacking. A number of nonspecific behavioral changes have been identified as potential indicators of acute illness including functional decline, loss of appetite, "not being one's self," agitation, weight loss, weakness, lethargy, and apathy, among others. No studies of reasonable quality have systematically evaluated nonspecific behavioral changes in relationship to infections among nursing-home residents. Limitations of the few studies conducted to date include (1) lack of generalizability stemming from sampling bias; (2) potential exposure misclassification resulting from failure to define a priori the behavioral changes of interest; (3) exposure ascertainment bias relating to reliance on sparse medical record documentation and/or retrospective design; and (4) outcome misclassification bias from failing to adequately define outcomes using accurate diagnostic criteria.[22,33,76,84-93] No studies assessed the ability of nonspecific behavioral changes to discriminate between individuals having an acute illness due to infection versus alternative causes. Boockvar et al[81,92] evaluated the ability of nonspecific behavioral symptoms to predict all cause acute illnesses in 2 studies conducted at a single academically affiliated nursing home. The first used a consensus-based assessment tool developed from focus group interviews of nursing assistances, nurses, and physicians. Daytime nursing assistants completed the tool daily. The tool had a sensitivity of 53%, a specificity of 96%, but an overall positive predictive value of only 17%. In the second study, the researchers examined the ability of nonspecific behavioral symptoms identified in nursing notes to identify acute illnesses in general. Again, the overall positive predictive value of any behavioral changes was only 24%, though the negative predictive value was 91%.[94] Acute illnesses occurred frequently among residents in this study; roughly 12.5% of residents during each 10-day study interval. The low PPV in these studies would likely result in unnecessary additional clinical assessments. Moreover, these studies relied on having a stable and consistent staff with strong knowledge of each resident's baseline condition. If applied to other settings, the performance of the instruments would likely be lower.

Given the difficulties in establishing whether a behavioral change is present and the lack of data supporting a linkage with infection, clinicians should not pursue an evaluation for infection when presented with a nursing-home resident experiencing behavioral changes in isolation. It is reasonable perform active monitoring of these residents so that additional signs and symptoms of infection may be identified early.[95] Further evaluation for infection may be merited in those situations where additional, more specific signs and symptoms develop.

Functional decline
Should identification of new-onset functional decline in a nursing home resident prompt further evaluation for the presence of infection? **Recommendation:** We do not recommend that clinicians further evaluate a resident with new-onset functional decline for the presence of infection.

Rationale: Strong evidence exists for an association between infection and decline in functional status of older adults,[96] and functional decline is included as a criteria for establishing the presence of infection in recently updated surveillance definitions[21]; however, functional decline appears to be both a risk factor as well as an outcome of infection.

The utility of functional decline as a leading indicator of infection is unclear. Ferrucci et al[97] evaluated community-dwelling older adults for changes in activities of daily living (ADLs). Among residents who were independent in their ADLs at baseline, these researchers found that >70% of individuals who developed severe disability were hospitalized in the same year. Pneumonia was the fourth most common reason for hospitalization, preceded by stroke, hip fracture, and congestive heart failure.[97] Using Medicare and MDS assessments, Kruse et al[98] assessed changes in ADLs for a large cohort of nursing homes residents before and after hospitalization.[98] With the exception of hip fractures, which were sometimes associated with recovery of ADLs, they found that most hospital admissions led to both a decrease in function and a more rapid rate of subsequent decline. Pneumonia was the most common reason for admission among the entire cohort (33.5%). For those with mild ADL impairment at baseline, the next most common reasons for hospitalization were hip fracture (18.9%) and congestive heart failure (17.4%). Among those with severe ADL impairments, the hospital diagnosis was septicemia (25.0%) and UTI (19.0%).[98] Bula et al[99] prospectively assessed changes in ADLs among residents of nursing homes who developed an infection. Similar to Kruse et al,[99] they determined that infections led to a more precipitous decline in function and that

those with greater impairment at baseline were more likely to develop an infection.[99]

Although a large number of methods are available for measuring functional status, functional status in nursing homes is most commonly measured using ADLs because it is a required component of periodic assessments in MDS version 3.0.[100] The MDS ADL measure assesses resident physical function on a scale ranging from 0 to 28 based on level of dependency in 7 self-care related activities: dressing, bathing, hygiene, toileting, transfers, mobility, and eating. A significant decline in functional status, defined as a ≥3-point increase on the MDS ADL scale, is 1 of 4 potential constitutional symptoms (including fever, delirium, and leukocytosis) used to establish the presence of infection in recently published nursing home infection surveillance guidelines.[27]

We had extensive conversations about the utility of functional decline as an indicator of infection. The literature search conducted for this manuscript did not identify studies that established functional decline as useful tool for prospectively identifying infection in nursing homes. The MDS ADL measure, as currently operationalized in nursing homes, is calculated based on observations performed over a 7-day period, which makes it impractical as a timely leading indicator of infection. Moreover, functional decline is associated with a number of other noninfectious disorders,[97,98] which limits its specificity for infection. Given these issues, we do not recommend that clinicians pursue an evaluation for infection when presented with a nursing-home resident experiencing isolated decline in functional status. Clinicians should consider a period of active monitoring for nursing-home residents with abrupt functional decline.

Falls

Should a fall in a nursing home resident prompt further evaluation for the presence of infection? **Recommendation:** We do not recommend that clinicians evaluate a resident who has experienced a fall for the presence of infection.

Rationale: Falls are common among older residents of nursing homes. Although many factors account for falls, they often prompt an infectious work-up and/or empiric antibiotic treatment for suspected infection, specifically, UTIs. A cross-sectional study conducted in residents of nursing homes found that patients who fell had positive urine cultures as often as those who did not fall[101] Another prospective cohort study of residents of nursing homes in the United States described a negative association between falls and bacteriuria accompanied by pyuria ($\chi^2 = 6.69$, df = 1, $P = .01$).[102] Our literature search did not identify studies that evaluated the association between falls and other infectious syndromes such as pneumonia. Therefore, we determined that insufficient evidence exists to estimate the likelihood of infection in residents of nursing homes who have fallen.

Anorexia

Should new-onset anorexia a nursing home resident prompt further evaluation for the presence of infection? **Recommendation:** We do not recommend that clinicians further evaluate a resident with new-onset anorexia for the presence of infection.

Rationale: In a prospective, observational study of residents of a nursing home, the development of new-onset anorexia was independently associated with the subsequent onset of acute illness [positive predictive value (PPV), 0.46; likelihood ratio (LR), 6.0].[94] In this study, infections were the most commonly identified acute illness, although these researchers did not specifically examine the relationship between anorexia and infection. In another prospective study performed in 22 Swedish nursing homes, bacteriuria was lower among residents with new onset anorexia than in residents without anorexia (18% vs 33%; $P = .15$), although this difference did not achieve statistical significance.[72] Residents with anorexia were more likely to have received an antibiotic in the month prior to urine testing, which suggests the medication, rather than an infection, had triggered this nonspecific symptom. Further evaluation for infection does not appear to be routinely merited based on the findings of these limited studies, particularly when this symptom is present in isolation; however, it is reasonable to monitor residents with new onset anorexia closely to identify development of additional signs and symptoms that may point to infection[95] and, if developed, may prompt further evaluation for infection.

In conclusion, this expert guidance document was developed to guide clinicians in diagnosing infection in residents of nursing homes who exhibit nonlocalizing signs and symptoms to minimize inappropriate antimicrobial prescribing and use. It provides the foundation for common infection definitions and discusses which nonlocalizing signs and symptoms should be incorporated into clinical criteria for initiation of antibiotics in residents of nursing homes.

The guidance should not replace clinical judgement when caring for residents of nursing homes with a suspected bacterial infection. Although some nonlocalizing signs and symptoms, such as fever and delirium, are associated with infection, we emphasize that clinicians should consider the possibility of noninfectious causes that may be equally or more likely responsible (eg, dehydration as a cause of change in mental status (exclusive of delirium), low blood pressure in a resident with suspected orthostatic hypotension). Additionally, the isolated presence of any one nonlocalizing sign and/or symptom should not lead to antibiotic therapy. Clinicians should consider the presence of nonlocalizing signs or symptoms in the context of a resident's clinical presentation.

In this document, we have described the diagnostic value of nonspecific signs and symptoms in residents of nursing homes. Residents with nonspecific signs or symptoms, such as decline in functional status in combination with other findings suggestive of infection (eg, dysuria), may need further evaluation to determine whether infection is present and whether or which treatment is needed. We emphasize that nonspecific signs or symptoms presenting alone in a resident should not automatically prompt a clinician to evaluate the resident for infection.

Finally, successful application of this expert guidance document's recommendations depends on frontline staff members' abilities to access recommended tools and appropriately apply them to residents presenting with 1 or more of these signs and symptoms. Facilities should evaluate whether their frontline personnel have access to and training for such tools as the CAM criteria and should make changes accordingly to support frontline staff access and understanding.

Future Research

The recommendations from this document are based on expert opinions informed by existing literature. The body of research on this topic largely consists of observational trials. We urge researchers to pursue randomized trials to assess the impact of approaches to evaluation, as well as treatment of, infections in nursing-home residents.

Supplemental material. To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2020.1282

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