Research Article

Determining Appropriateness of Antibiotic Therapy in Nursing Home Residents: A Review

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Upwards of 70% of nursing home residents receive at least one course of antibiotics yearly but as many as 75% of these courses have been considered inappropriate. In response to this potential overprescribing of antibiotic nursing homes are now required to have an antimicrobial stewardship program to monitor and improve prescribing. However, determining appropriateness of antibiotic therapy in the nursing home setting has been a major challenge. The objectives of this review were to identify and review studies of appropriateness of antibiotic therapy in nursing homes with special focus on the criteria utilized for determining appropriateness. Of the 30 studies identified in the literature review, 50% utilized infection surveillance definitions that were not designed to assess appropriateness of antibiotic therapy in individual residents. There was also variation in the size of study populations, study design, and criteria for identifying the study population. These limitations not only make comparisons among studies problematic but also raise concerns about the validity of the findings regarding the level of appropriateness of antibiotic prescribing in nursing homes. Suggestions are provided for the design of future studies of antibiotic appropriateness in nursing homes that focus on standardizing the methodology to minimize the variation observed in the studies in this review.

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Running Head: Determining Appropriateness of Antibiotic Therapy in Nursing Home Residents

Introduction

In the past two decades there has been an increasing focus on evaluating the appropriateness of antibiotic therapy in the nursing home setting due to several factors. First, upwards of 70% of residents in nursing homes receive at least one course of antibiotics yearly[1][2][3][4][5]. Second, as many as 75% of antibiotic prescriptions in nursing home residents have been considered inappropriate[6][7][8][9][10][11]. Third, unnecessary antibiotic therapy can result in adverse drug reactions, *C. difficile* infection, and development of antibiotic resistance that can lead to increased healthcare costs, morbidity, and mortality[12][13]. In response to these issues the Centers for Medicare and Medicaid Services (CMS), in its recently published revision of the conditions of participation regarding infection control requirements, required long-term care facilities to have an antimicrobial stewardship program that includes protocols and monitoring for antibiotic use[14]. To assist nursing homes in meeting CMS requirements the

Centers for Disease Control and Prevention (CDC) developed core elements for antimicrobial stewardship in nursing homes of which one component is Identifying inappropriate use of antibiotics and implementing interventions to improve use[15].

However, determining appropriateness of antibiotic therapy in the nursing home setting has been a major challenge. An example of this challenge is identifying residents with symptomatic urinary tract infection (UTI) that has resulted in publication of multiple decision tools for the diagnosis and treatment of UTI in the nursing home setting[16]. But these efforts are hindered by two factors: lack of a gold standard for the diagnosis of UTI in residents and no standardized criteria for the clinical diagnosis of this infection[16]. Previously, considerable variability in definitions and methods for evaluating appropriateness in the hospital setting was identified that creates concerns about the results of studies evaluating appropriateness of antibiotic therapy in nursing home residents[17].

Therefore, the objectives of this review are: a) to identify and summarize the findings of studies that evaluated appropriateness of antibiotic therapy in nursing home residents; b) to evaluate the methodology utilized for determining appropriateness of antibiotic therapy in these studies; and c) to provide suggestions for the design of future studies of appropriateness of antibiotic therapy in the nursing home setting.

Methods

After a resident's acute illness is evaluated and infection is suspected, the decision-to-treat is the initial, and most important, decision in the antibiotic prescribing event that includes choice of agent, choice of dose, modification of therapy (escalation, de-escalation, or stopping), and duration of therapy. Therefore, for the purposes of this review, the focus was on studies evaluating appropriateness of the decision-to-treat nursing home residents with suspected infection. A literature search was conducted using Google Scholar and Medline with Ovid from January 1, 1980 to March 31, 2022 to identify studies of appropriateness of antibiotic therapy in nursing home residents that focused on decision-to-treat published in English. Search terms included nursing home, long-term care, antibiotics, antimicrobial use, appropriateness, and antimicrobial management in various combinations. References of included studies were searched for additional studies not identified in the literature review. Letters to the editor, conference proceedings, commentaries, reviews, and studies that focused only on measuring antibiotic use in nursing homes without assessing appropriateness were excluded. Data abstracted from each study included: first author, year of the publication, country where the study was conducted, number of facilities studied, study years, study design, infections studied, criteria for identifying the study population, and results. The author conducted all literature searches and abstracted all the data included in this study.

After literature review, 30 studies met inclusion criteria and were classified into the following categories:

1. Studies of appropriateness of antibiotic therapy in nursing home residents conducted in the 1980s that used criteria developed by the authors as decision to treat criteria;

2. Studies of appropriateness of antibiotic therapy in nursing home residents that utilized infection surveillance definitions specifically designed for the nursing home setting[18][19] as decision to treat criteria;
3. Studies of appropriateness of antibiotic therapy that utilized criteria for the decision to initiate antibiotic treatment specifically designed for the nursing home setting [20] as decision to treat criteria;
4. Studies of appropriateness of antibiotic therapy in nursing home residents that compared infection surveillance definitions [18][19] and criteria for initiation of antibiotics [20] as decision to treat criteria; and
5. Studies of appropriateness of antibiotic therapy in nursing home residents published since 2000 that utilized alternative methods as decision to treat criteria not fitting into one of the other four categories.

Results

Studies of appropriateness of antibiotic therapy in nursing home residents conducted in the 1980s that used criteria developed by the authors as decision to treat criteria (Table 1)

The first studies of appropriateness of antibiotic therapy in nursing home residents were conducted in the 1980s[21][22][23][24]. Two studies published in the 1990s[23][24] utilized data collected in the 1980s and are included in this group. Differences in methodology were identified among these 4 studies including variation in the number of study facilities, study design, and how Infections were identified. Most importantly, there was variation in the criteria for appropriateness of antibiotic therapy. The variation in methodology resulted in a wide range of appropriateness of antibiotic therapy for common infections: UTI 18-65%, lower respiratory infection (LRTI) 16-85%, and skin/soft tissue infection (SSTI) 13-59%. Therefore, it is difficult to determine if any of these studies provide an accurate assessment of the appropriateness of antibiotic treatment in nursing home residents at the time the studies were conducted.

Author, year	Country	# Facilities	Study Years	Design	Infections Studied	Criteria for Infection Identification	Criteria for Appropriateness	Results
Zimmer, 1986[21]	United States	42 nursing homes in New York State	1982	Point Prevalence survey of residents on antibiotic treatment	All infections treated with systemic antibiotic (N = 173)	Modification by authors of CDC criteria for hospital surveillance UTI 58% LRTI 19% SSTI 5% ? Site 14%	Expert panel developed minimum criteria for initiating antibiotic treatment	Percent appropriateness based on meeting minimum criteria: All infections 62% UTI 65% LRTI 85%
Jones, 1987[22]	United States	2 nursing homes in Oregon	3 months in 1986	Retrospective chart review of residents receiving oral or parental antibiotic	Any infection treated with systemic antibiotic (N = 170)	Infection logs of infection control: UTI 52% LRTI 27% SSTI 15%	Expert panel used prior publications[26, 27] to evaluate appropriateness	Appropriateness of initial treatment: 49% appropriate 42% inappropriate 9% unjustified Appropriateness by site of infection: UTI 57% LRTI 50% SSTI 31%
Warren, 1991[23]	United States	52 nursing homes in Maryland	Feb 1985-	Longitudinal surveillance of 3,899	Surveillance for: UTI, LRTI,	2 methods of identifying infection:	Minimum criteria for diagnosis of	2,120 residents treated (54% of residents) with
			Jan 1986	residents for infection	SSTI, FUO, URI	Prescriber diagnosis	infection developed by	4,462 antibiotic courses

Author, year	Country	# Facilities	Study Years	Design	Infections Studied	Criteria for Infection Identification	Criteria for Appropriateness	Results
						(53%), or chart review for signs/sx reviewed by expert panel (43%); or no diagnosis (4%)	panel of 10 physicians	% Infections (%Appropriate) UTI 36% (18%) LRTI 16% (4%) SSTI 17% (13%) FUO 6% (2%)
Montgomery 1995[24]	Canada	100 facilities in Manitoba province	Fiscal 1986-87	Retrospective chart review of residents on antibiotic treatment	All infections	20% probability sample of antibiotic prescriptions (N = 979 prescriptions)	Minimum criteria of Zimmer et al[21] (no. (% of total prescriptions UTI 256 (26%) SSTI 253 (26%) LRTI 211 (23%)	% Appropriateness of treatment course by infection site: UTI 31% SSTI 59% LRTI 87% 57% of all courses met criteria for appropriateness

Table 1. Studies of appropriateness of antibiotic therapy in nursing homes using decision to treat criteria conducted in the 1980s

Abbreviations: *CDC = Centers for Disease Control and Prevention*; *UTI = urinary tract infection*; *LRTI = lower respiratory tract infection*; *SSTI = skin/soft tissue infection*; *FUO = fever of unknown origin*; *URI = upper respiratory infection*; *dx = diagnosis*; *signs/sx= signs/symptoms*

Studies of appropriateness of antibiotic therapy in nursing home residents that utilized infection surveillance definitions specifically designed for the nursing home setting [18][19] as decision to treat criteria (Table 2)

Surveillance definitions for infections specifically designed for nursing homes were first published in 1991 (McGeer criteria)[18] and revised in 2012 ("revised McGeer criteria")[19] with improvements in the specificity and positive predictive value of criteria for UTI and pneumonia[25]. It was explicitly stated in the revision that because of the specificity of the criteria they may not be adequate for use as diagnostic criteria for real-time diagnosis of infection and decision to initiate antibiotic therapy.

Utilization of the McGeer criteria [18]

Four studies were identified that utilized the McGeer criteria [18] to assess appropriateness of antibiotic therapy in nursing home residents[6][26][27][28]. There was variation in study design and infections evaluated among the four studies. The number of antibiotic courses evaluated in 3 studies was large: 662[28], 988[27], and 1,602[26] whereas only 172 episodes were included in a study of UTI[6]. In 3 studies, appropriateness of treatment based on the McGeer criteria[18] was 49%[26], 60%[27], and 37%[28]. In the study of UTI[6], only 15% (26/172) of episodes met McGeer criteria[18]. In 3 studies [26][27][28] the authors noted the limitation of using the McGeer criteria[18] for determining appropriateness of antibiotic therapy.

Utilization of the revised McGeer criteria [19]

Four studies were identified that utilized the revised McGeer criteria [19] to evaluate appropriateness of antibiotic therapy in nursing home residents[29][30][31][32]. The design of 3 studies [29][30][31] was retrospective and the fourth[32] was a randomized control trial (RCT) of an intervention to reduce antibiotic use in nursing. The infections evaluated in these 4 studies varied: pneumonia [29], UTI [30][31], and all infections[32]. The study population was small in all 4 studies. Inclusion criteria varied: chart documentation of infection [29], residents with a urine culture [30], treatment of presumed UTI [31], and antibiotic treatment for any infection[32]. In the pneumonia study [29], based on chart documentation of infection, the revised McGeer criteria was fulfilled in 84/108 episodes (78%}. Excluding the study of pneumonia [29], in 3 studies [30][31] that utilized different methodology for determining the study population, a low percentage of episodes met revised McGeer criteria for appropriateness of treatment (9-18%).

The validity of the 8 studies of appropriateness of antibiotic therapy determined by application of the McGeer [18] or the revised McGeer criteria [19] is a concern. First, there was variation in the criteria for determining the study population illustrated by the 5 studies evaluating treatment of UTI: identification of infection by an infection control nurse [26]; residents with a positive urinalysis[6]; suspected infection by nursing staff [28];

residents with a urine culture [30]; and, infection logs indicating treatment [31]. Second, 5 of the 8 studies had a retrospective design. The lack of chart documentation of signs and symptoms of infection noted in one retrospective study [30] illustrates the difficulty of evaluating appropriateness of therapy using this design. Lastly, the revised McGeer criteria [19] were utilized despite the caveat in the paper describing these criteria that they were not designed for clinical diagnosis of infection and decision-making regarding antibiotic therapy.

Author, year	Country	# Facilities	Study Years	Design	Infections Studied	Criteria for Inclusion in study	Results
Studies that utilized the original McGeer criteria[18]							
Loeb 2001[26]	Canada	22 nursing homes; 2,408 residents; 9,373 antibiotic courses	Nov 96-Oct 97	Prospective	LRTI, UTI, SSTI	1,602 antibiotic courses for LRTI, UTI, and SSTI based on ICP chart review	Overall, 49% of antibiotic courses met criteria for treatment Appropriateness of treatment by infection: LRTI 58% UTI 28% SSTI 65%
Rotjanapan 2011[6]	United States	2 nursing homes in Rhode Island	June-Nov 2008	Retrospective chart review	UTI	Review of 172 charts of residents without foley who had positive urinalysis	Overall, 15% (N = 26) met McGeer criteria [18] for UTI and all were treated with an antibiotic Of the 85% (N = 146) not meeting criteria, 70 (41%) received treatment; no hospitalizations or deaths occurred in those not treated
Stuart 2012[27]	Australia	5 nursing homes	July 2009August 2011	Retrospective review of infection control treatment logs	All infections	988 Antibiotic courses during the study period	Overall, 596 (60%) antibiotic courses met McGeer criteria[18]. Among the 5 facilities, the range for meeting criteria was 57-70%.
Lim 2012[28]	Australia	4 nursing homes	2009-2010	Prospective evaluation of suspected	All infections	662 episodes of suspected infection by	415 (37%) episodes of suspected infection met

Author, year	Country	# Facilities	Study Years	Design	Infections Studied	Criteria for Inclusion in study	Results
				infection by the ICP		staff and had antibiotic treatment	McGeer criteria[18] for treatment Appropriateness of treatment courses by infection: LRTI 33% UTI 49% SSTI 33%
Studies that utilized the revised McGeer criteria[19]							
Zimmerman 2016[29]	US	16 nursing homes in North Carolina	JulDec 2013	Retrospective review of 1,089 records	Pneumonia	3 criteria for pneumonia: 1. diagnosis in chart; 2. revised McGeer criteria[19]; 3. treated with antibiotic used for pneumonia	Overall, 108 of 1,089 (9.9%) cases met one of the diagnostic criteria # cases /1000 RCD varied by criterion: Clinical diagnosis: 0.71/1000 Revised McGeer: 0.56/1000 Antibiotic prescribed: 0.32/1000 Clinical diagnosis identified 107/108 (99%) Revised McGeer identified 84/108 (78%) Antibiotic identified 47/108 (44%) Conclusion: Written documentation of diagnosis of pneumonia

Author, year	Country	# Facilities	Study Years	Design	Infections Studied	Criteria for Inclusion in study	Results
							identified 99% of cases identified by any of the 3 criteria
Sloane 2017[30]	United States	31 nursing homes in North Carolina	Nov 2014Mar 2015	Retrospective review of charts (N = 254)	UTI	Chart review by research staff of a random selection of residents with urine cultures	46 (18%) of 254 residents met revised McGeer criteria[19] for UTI; 19 (41%) of 46 started on empiric treatment; Of 178 residents not started on empiric treatment, 111 (62%) had a positive urine culture; 14 (13%) of the 111 met revised McGeer criteria[19] for UTI
Khatri 2021[31]	Australia	6 nursing homes	March, April, May 2019	Retrospective audit of antibiotic treatment of presumed UTI	UTI	Infection logs indicating treatment for UTI (N = 74)	Applying revised McGeer criteria[19]: 10 (13%) met clinical and micro criteria 15 (20%) met clinical criteria only 34 (46%) met micro criteria only (ASB) 15 (20%) no criteria met 66% of those treated did not meet clinical criteria

Author, year	Country	# Facilities	Study Years	Design	Infections Studied	Criteria for Inclusion in study	Results
Fleet 2014[32]	United Kingdom	30 nursing homes in London	Jan 2010May 2011	Cluster RCT of an intervention to reduce antibiotic use in NHs	All infections	PPS of antibiotic treatment in intervention and control groups	% Episodes meeting McGeer[18] and revised McGeer criteria[19] before (N = 139) and after intervention (N = 135) in intervention group: Before After McGeer 9.4 % 11.1 % Revised McGeer 9.4% 10.4%

Table 2. Studies that utilized surveillance definitions specifically designed for the nursing home setting[18][19] as decision to treat criteria to evaluate appropriateness of antibiotic therapy

Abbreviations: *UTI = urinary tract infection; LRTI = lower respiratory tract infection; SSTI = skin/soft tissue infection; U/A = urinalysis; ICP = infection control preventionist; micro = microbiologic; ASB = asymptomatic bacteriuria; RCT = randomized controlled trial; PPS = point prevalence survey*

Studies of appropriateness of antibiotic therapy that utilized criteria for the decision to initiate antibiotic treatment specifically designed for the nursing home setting [20] as decision to treat criteria (Table 3)

An expert panel developed minimum criteria for initiating antibiotic treatment in nursing home residents with suspected infection (referred to as the "Loeb criteria" or "Loeb minimum criteria") to specifically assist physicians in decision-making regarding antibiotic prescribing [20]. A clear distinction was made between infection surveillance definitions and minimum criteria for initiating antibiotic therapy. Non-localizing signs (change in mental status, falls, decreased appetite, etc.) were not included in the criteria because of poor specificity even though they may occur with infection in residents. Hughes et al [33] in the United Kingdom published a guideline for the identification of UTI, LRTI, and SSTI in nursing home residents based on a revision of the Loeb criteria [20] but

no studies evaluating its use were identified in the literature review.

Six studies were identified that utilized the Loeb criteria [20] to evaluate appropriateness of antibiotic therapy in nursing home residents[11][34][35][36][37][38]. There was variation in study design, infections evaluated, and size of the study population among these 6 studies. In 3 studies of UTI [35][36][37] inclusion criteria varied but the percentage of cases that met Loeb criteria [20] was low: 16% [35], 8% [36], and 17% [37]. In the 2 studies that evaluated treatment of UTI, LRTI, and SSTI [11][34], the findings regarding meeting Loeb criteria [20] differed: 12.7% [34] and 53% [11]. In the study of all infections [38], 41% of antibiotic prescriptions met Loeb criteria [20]. Overall, of the 6 studies that utilized the Loeb criteria to assess appropriateness of antibiotic therapy, only one [11] had a level of appropriateness > 50%. Appropriateness levels for UTI ranged from 8-44% in the 6 studies.

Author, year	Country	# Facilities	Study Years	Design	Infections Studied	Criteria for Inclusion in study	Results
Olsho 2013[34]	United States	12 nursing homes in North Carolina	Mar-May 2011	Retrospective chart audit of residents on antibiotic treatment (N = 653 prescriptions)	UTI, LRTI, SSTI	Antibiotic treatment for UTI, LRTI, or SSTI	Overall, only 12.7% of all prescriptions met Loeb criteria[20] Loeb criteria met by infection: UTI 10.2% LRTI 1.9% SSTI 42.7%
D'Agata 2013[35]*	United States	25 nursing homes in MA	Sept 2009-Nov 2011	Prospective study of 266 residents with advanced dementia	UTI	Suspected UTI based on chart report of UTI by MD, NP, PA, or nurse	72 (27%) of 266 residents had 131 suspected UTIs (10 with UC) 21 (16%) of 131 episodes met Loeb criteria[20] for treatment 15 of 21 episodes that met criteria had a positive U/A and culture
Doernberg 2015[36]	United States	3 nursing homes in California	Sept 2011-May 2912	Quasiexperimental study to assess an intervention to improve	UTI	Documentation of treatment for UTI by infection control and in medical record	104 of 183 treated UTI episodes during the intervention period were evaluated for initial appropriate treatment
				treatment of UTI			Only 8% of 104 met Loeb criteria[20] for

Author, year	Country	# Facilities	Study Years	Design	Infections Studied	Criteria for Inclusion in study	Results
							initiating antibiotic treatment
Kistler 2017[37]	United States	31 nursing homes in North Caroloina	Nov 2014-Mar 2015	Retrospective chart review of random selection of residents treated for UTI (N = 260 cases)	UTI	Infection logs documenting treatment for UTI	Of 260 cases, 106 (41%) had at least 1 Loeb criteria[20] but only 43 (17%) met all criteria
Penney 2018[38]	Canada	10 nursing homes in Newfoundland	Jan 2015-Jan 2016	Retrospective chart review of random selection of 448 antibiotic prescriptions	All infections	Residents on antibiotic treatment	Of 448 prescriptions, 41% met Loeb criteria[20] Loeb criteria met by infection: UTI 48/163 (29%) LRTI 62/140 (44%) SSTI 53/68 (78%)
Pulia 2018[11]	United States	5 nursing homes in Wisconsin	Jan 2013=Sept 2014	Retrospective chart review of residents on antibiotic treatment	UTI, LRTI, SSTI	Treatment for UTI, LRTI, or SSTI or met sepsis criteria[39][40]	Of 640 prescriptions, 53% N = 336) were appropriate Of 336 appropriate courses, 99 (29%) met sepsis criteria % appropriate by infection type: UTI (N = 324) 44%

Author, year	Country	# Facilities	Study Years	Design	Infections Studied	Criteria for Inclusion in study	Results
							LRTI (N = 94) 48% SSTI (N = 29) 78%

Table 3. Studies that utilized the Loeb criteria[20] as decision to treat criteria to evaluate appropriateness of antibiotic therapy in nursing home residents

* *In this study mental status and rigor were added to the Loeb criteria[20] by the authors because of the limited ability of residents with advanced dementia to express other symptoms localizing to the urinary tract.*

Abbreviations: *UTI = urinary tract infection*; *LRTI = lower respiratory tract infection*; *SSTI = skin/soft tissue infection*; *MA = Massachusetts*; *NP = nurse practitioner*; *PA = physician assistant*; *UC = urinary catheter*; *U/A = urinalysis*

Studies of appropriateness of antibiotic therapy in nursing home residents that compared infection surveillance definitions [18][19] and criteria for initiation of antibiotics [20] as decision to treat criteria (Table 4)

Seven studies were identified that compared the McGeer [18][19] and Loeb [20] criteria in the evaluation of the appropriateness of antibiotic therapy in nursing home residents [41][42][43][44][45][46][47]. There was variation in study design (prospective evaluation [41][42][47], retrospective chart review [43][44], and post hoc analyses of prospectively collected data [45][46] and infections studied (UTI [41][45][46], pneumonia and UTI [42], pneumonia only [43], SSTI [44], and UTI, LRTI, and SSTI [47]). There was variation in the identification of the study population in the UTI studies (suspicion of UTI by a physician or nurse plus urinalysis and culture [41], independent chart review verifying treatment for UTI [45], and a clinical diagnosis of catheter-associated UTI [46]) and the pneumonia studies (documented infection in the chart plus > 5 days of antibiotic treatment [42] or residents with a chest radiograph [43]). Overall, with the exception of one study [47], the study populations were relatively small.

Two studies [41][42] compared the McGeer [18], and Loeb criteria [20] and in both studies most of the suspected infections did not meet either criteria. One study [45] that compared the revised McGeer [19] and Loeb criteria [20] in assessing treatment of UTI also utilized an algorithm developed by Crnich and Drinka [48] to evaluate appropriateness of treatment. This algorithm was based partly on criteria published by Loeb et al [20]. However, a unique aspect of this algorithm is the option to initiate empiric antibiotic therapy if there is a change in status of a resident associated with one or more specific "warning signs" (fever, rigors, delirium, or unstable vital signs) in the absence of localizing urinary signs and symptoms of UTI. The algorithm [48] is the foundation of a recently

published multicomponent toolkit to improve the diagnosis and management of UTI in nursing home residents [49].

In 5 of the 7 studies the percentage of episodes that met Loeb criteria [20] was consistently higher than for the revised McGeer criteria [19]. However, interpretation of the findings of these studies is limited because infection was identified based on chart documentation [42][45][46] or treatment with an antibiotic [44][47] and there is no way to independently determine the validity of the diagnosis.

Author, year	Country	# Facilities	Study Years	Design	Infections Studied	Criteria for Inclusion in study	Results
Juthani-Mehta 2007[49]	United States	3 nursing homes in Connecticut	May 2005-April 2006	Prospective surveillance of 340 residents for suspected UTI	UTI	Physician or nurse clinically suspected UTI and U/A and culture were done	100 residents suspected to have UTI; 43 (43%) had positive U/A and culture Operating characteristics of each criteria for positive U/A and culture: Sen Spec PPV NPV McGeer[18] 30% 82% 57% 61% Loeb[20] 19% 89% 57% 59%
Wang 2012[50]	United States	15 nursing homes In Michigan	No dates stated	Prospective surveillance of residents for infection with and without indwelling devices	Pneumonia and UTI	Documented infection in chart plus ≥5 days of antibiotic treatment	146 pneumonia and UTI cases (72 with and 74 without a device); Device No Device Total cases 72 74 N (%) McGeer[18] 8 (11) 15 (20) N (%) Loeb[20] 12 (17) 10 (14) N (%) Either 13 (18) 18 (24)

Author, year	Country	# Facilities	Study Years	Design	Infections Studied	Criteria for Inclusion in study	Results
Brown 2016[51]	United States	31 nursing homes in North Carolina	Nov 2014March 2015	Retrospective chart review of 226 residents	Pneumonia	Residents with chest radiograph ordered	Of 226 CXR, 118 (52%) read as unlikely pneumonia; 67 (30%) highly likely, and 41 (18%) ambiguous N (%) of cases meeting criteria: Revised McGeer [19] 15 (7) Loeb[20] 68 (30)
Feldstein 2017[52]	United States	31 nursing homes in North Carolina	Sept 2014March 2015	Retrospective chart review	Skin/soft tissue	Treatment for SSTI based on logs provided by each NH	70% of treatment courses initiated in NH; 30% courses ordered in non-NH settings. N (%) cases meeting criteria: Revised McGeer [19] 40 (25) Loeb criteria [20] 77 (48)
Eure 2017[53]	United States	9 nursing homes in 4 states	Dec 2013May 2014	Post-hoc analysis of 1day point prevalence survey of treatment for UTI	UTI	Treatment determined to be for UTI by independent chart reviewers	On the survey day, 33 residents were on treatment for UTI 3 algorithms applied to determine appropriateness of treatment: N (% appropriate) Loeb criteria[20] 10 (30)

Author, year	Country	# Facilities	Study Years	Design	Infections Studied	Criteria for Inclusion in study	Results
							Revised McGeer [19] 5 (15} Crnich/Drinka[56] 15 (45)
Armbruster 2017[54]	United States	12 nursing homes in Michigan	May 2010- April 2013	Post-hoc analysis of CRT of 233 residents with UC	UTI	Residents with clinical diagnosis of CAUTI	182 cases of CAUTI with complete data N (%) cases meeting criteria: Loeb[20] 74 (40) Revised McGeer [19] 59 (32) Either criteria 91 (50)
Uribe-Cano 2021[55]	United States	5 nursing homes in Wisconsin	Jan 2013Sep 2014	Prospective evaluation of residents prescribed an antibiotic	UTI, LRTI, SSTI	Residents on treatment for UTI, LRTI, or SSTI	734 of 1,442 antibiotic courses were for: UTI (363), LRTI (206), and SSTI (165) N (%) of all cases meeting criteria: Loeb[20] 372 (52) Revised McGeer [19] 211 (29) Either criteria 412 (56) N (%) cases meeting criteria by infection type:

Author, year	Country	# Facilities	Study Years	Design	Infections Studied	Criteria for Inclusion in study	Results
							Loeb[20] Revised McGeer [19] UTI 130 (36) 100 (28) LRTI 123 (60) 51 (25) SSTI 119 (72) 60 (36)

Table 4. Studies comparing the McGeer[18][19] and Loeb criteria[20] for the evaluation of appropriateness of antibiotic therapy in nursing home residents.

Abbreviations: *U/A = urinalysis; Rev Loeb = revised Loeb criteria;[38] Sen = sensitivity; Spec = specificity; PPV = positive predictive value; NPV = negative predictive value; UTI = urinary tract infection; CAUTI = catheter-associated urinary tract infection; LRTI = lower respiratory tract infection; SSTI = skin/soft tissue infection; UC = urinary catheter; CXR = chest x-ray; CRT = cluster randomized trial*

Studies of appropriateness of antibiotic therapy in nursing home residents published since 2000 that utilized alternative methods as decision to treat criteria not fitting into one of the other categories (Table 5)

Five studies published between 2008 and 2018 were identified that utilized other methods for defining appropriateness of the decision to treat in nursing home residents that differed from other studies published during this time period[7][50][53][54][55]. In two studies [7][50] a different method for assessing appropriateness of treatment was used compared to previously published studies but no rationale was given for this approach. In the other 3 studies, national [53][54] or regional [55] guidelines were used to assess appropriateness but these studies only have relevance to the countries in which the study was done.

Author, year	Country	# Facilitie s	Study Years	Design	Infections Studied	Criteria for Inclusion in study	Criteria for Appropriate -ness	Results
Zabarsky 2008[50]	United States	1 VA nursing home	Feb 2002Oct 2004	Prospective study of an intervention to reduce abx rx of ASB	UTI	All residents included with or without urinary catheter	2 reviews of UTI in NHs[51][52]	# ASB # (%) Rx ASB Rx Pre-Inter 34 23 (68) Post-Inter 1-6 mo 26 18 (69) 7-30 mo 75 33 (44)
Peron 2013[7]	United States	1 VA nursing home	Oct 2008Mar 2009	Retrospective review of 100 randomly selected abx courses	All infections	Treated with an antibiotic	2 ID specialists determined if abx necessary using IDSA practice guidelines[a]	Of 100 abx courses, 42 unnecessary; Of 58 necessary courses, part of regimen unnecessary in 22 (20 duration too long)
van Buul 2015[53]	Netherlands	10 nursing home	Jan 2012Oct 2012	Prospective	UTI, RTI, SSTI	Form completed by NH physician for suspected infection	Algorithms developed by research team and expert panel based on	598 cases: UTI 356 (60%), RTI 208 (35%), SSTI 34 (5%) % RX Appropriate Overall 76%

Author, year	Country	# Facilitie s	Study Years	Design	Infections Studied	Criteria for Inclusion in study	Criteria for Appropriate -ness	Results
								UTI 68% RTI 87%
							Dutch guidelines and Loeb criteria[20]	SSTI 94%
Lemoine 2018[54]	France	137 nursing homes in HautsdeFrance region	June-Dec 2015	Prospective	UTI	Residents ≥ 75 with dx of suspected UTI	2014 UTI guideline by French Infectious Diseases Society	444 suspected UTI episodes based on MD diagnosis 10% of suspected episodes met French guideline for UTI dx After reclassification of episodes using the French guideline, 79% of episodes were considered infections requiring treatment
Lee 2018[55]	Canada	7 nursing homes in Sas-katchewan	May-July 2017	Prospective before/after intervention	UTI	Residents with positive urine culture	Local health region's diagnostic criteria for	Pre-Inter Post-Inter # UC 172 151 # (%) UC

Author, year	Country	# Facilitie s	Study Years	Design	Infections Studied	Criteria for Inclusion in study	Criteria for Appropriate -ness	Results
							UTI[b]	pos 62 (36) 50 (33) # (%) pos UC with criteria 12 (19) 15 (30) # (%) ASB 50 (81) 35 (70) # (%) ASB Treated 45 (90) 22 (63)

Table 5. Studies published since 2000 that utilized various other criteria to assess appropriateness of antibiotic therapy

[a] *Infectious Diseases Society of America. [Accessed April 24, 2012] Standards, practice guidelines, and statements developed and/or endorsed by IDSA. Available at: http://www.idsociety.org/Index.aspx.*

[b] *Appears to be a modification of the Loeb criteria[20] but not clearly stated in the paper*

Abbreviations: *abx = antibiotic; rx = treatment; ASB = asymptomatic bacteriuria; dx = diagnosis; Pre-inter = pre-intervention; PostInter = Post-Intervention; UTI = urinary tract infection; LRTI = lower respiratory tract infection; RTI = respiratory tract infection; SSTI = skin/soft tissue infection; Complic = complicated; ASB = asymptomatic bacteriuria; UC = urine culture; pos = positive*

Additional analysis of studies utilizing the McGeer [18], revised McGeer [19], and Loeb criteria [20]

Twenty-one of 30 studies used the McGeer [18], revised McGeer [19], or Loeb criteria [20] alone or in combination for evaluating appropriateness of antibiotic therapy. Appropriateness of therapy utilizing these 3 criteria by infection type is shown in Table 6. UTI was most often evaluated for appropriateness of treatment and there was variability in appropriateness for each of the 3 criteria. The variability is demonstrated best in the 9 studies that utilized the Loeb criteria in which appropriateness for treatment of UTI varied from 8% to 44%. Overall, the findings in Table 6 demonstrate the variation in level of appropriateness of antibiotic treatment for a specific infection when each of the 3 criteria is utilized.

Infection (s) Studied	McGeer Criteria[18]	Revised McGeer criteria[19]	Loeb criteria[20]
UTI	28[26] 15[6] 51[29]	18[30] 13[31] 15[45] 32[46] 28[47]	10[34] 29[38] 16[35] 44[11] 8[36] 30[45] 17[37] 40[46] 36[47]
Pneumonia	ND	78[29] 7[43]	30[43]
SSTI	65[26] 33[28]	25[44] 36[47]	43[34] 78[38] 78[11] 48[44] 72[47]
LRTI	33[28] 58[26]	25[47]	1.9[34] 44[38] 48[11] 60[47]
LRTI, UTI, SSTI**	49[26]	29[47]	12.7[34] 53[11] 52[47]
All Infections**	60[27] 37[28] 10.2[32]	9.9[32]	41[38]

Table 6. Comparison of the McGeer criteria[18], revised McGeer criteria[19], and Loeb criteria[20] for determining appropriateness of antibiotic therapy in 21 studies in nursing home residents*

**Data are percent appropriate treatment [reference]*

***Overall percentage appropriateness for infections in the study*

ND = not done

Discussion

Review of the literature for the last 35 years identified 30 studies evaluating appropriateness of the decision-to-treat suspected infection in nursing home residents. The findings can be summarized as follows. First, initial studies conducted in 1980s (Table 1) utilized different criteria for appropriateness that resulted in a wide range of appropriateness of antibiotic therapy that did not provide an accurate assessment of antibiotic therapy at that time. Second, 15 (50%) of the 30 studies that utilized infection surveillance definitions[18][19] to assess appropriateness of antibiotic therapy consistently found low levels of appropriateness. Third, the Loeb minimum criteria [20], developed to assist physicians in the decision-to-treat residents with suspected infection, tended to have a higher percentage of appropriateness compared to infection surveillance definitions [18] [19] but demonstrated considerable variability in the level of appropriateness (Table 6). Thus, the variation in methodology and results of the studies reviewed raise concern that they do not provide an accurate assessment of appropriateness of antibiotic prescribing in nursing home residents.

Why is there so much variability in studies of appropriateness of antibiotic therapy when using surveillance definitions or the Loeb criteria [20], especially since the Loeb criteria was developed to improve antibiotic prescribing in the nursing home setting? Infection surveillance definitions[18][19] and the Loeb criteria [20] utilize only localizing signs and symptoms for the diagnosis of infection and exclude the use of non-localizing signs and symptoms because they lack specificity. However, clinicians in the nursing home setting often prescribe antibiotics based solely on the presence of non-localizing signs or symptoms. This has been a particular concern in the diagnosis of UTI because non-specific signs and symptoms, e.g., results of a urinalysis, fever, falls, or change in mental status, are often the most common reason for considering this diagnosis[56][57]. Almost a decade ago it was suggested that non-localizing signs and symptoms be considered for inclusion in criteria for initiating antibiotic therapy in nursing home residents but apparently this did not gain acceptance [58]. However, interest has recently reemerged regarding non-localizing signs and symptoms as manifestations of infection in nursing home residents specifically focused on the association between delirium and UTI[59][60][61][62]. The rationale for this focus is the long-standing dogma that an acute change in mental status is an atypical manifestation of UTI in nursing home residents[60][63][64]. Three systematic reviews of the association between delirium and UTI in the elderly have been published[59][61][62]. The first review found an association between delirium and UTI but methodological flaws were identified resulting in the potential for bias [59]. A review of 22 studies concluded there was insufficient evidence to confirm an association between delirium and UTI because of varying definitions of confusion and criteria for the diagnosis of UTI and lack of control of confounding factors[61]. The most recent review of 29 studies found considerable heterogeneity and significant potential for bias but still concluded that there was an association between delirium and UTI [62]. However, only 3 studies in the latest review [62] were included in the prior

review [61] and this could explain, in part, the differing conclusions of these two reviews. In the author's opinion, because of the discordant results of these reviews[59][61][62], it remains unresolved regarding the association between delirium and UTI.

Notwithstanding the contradictory findings regarding the association of confusion and UTI, the relationship between acute change in mental status and infection in nursing home residents has been recently evaluated from the infection surveillance perspective. This was the subject of a *post hoc* study of data collected as part of a prevalence survey of infections in 161 nursing homes in the United States[65]. The revised McGeer criteria [19] was utilized to identify infection and the Confusion Assessment Method (CAM) was used to define an acute change in mental status[66]. The CAM consists of 4 elements that must be present for the diagnosis of delirium. The authors also evaluated what was termed "possible acute change in mental status" defined as documentation of any one of the 4 CAM elements. Of 15,276 residents' charts reviewed, none met the full CAM criteria for acute mental status change but 296 (1.9%) had at least one element of the CAM documented. The prevalence survey identified 161 infections using the revised McGeer criteria [19] and addition of the "possible acute change in mental status" criterion identified an additional 21 infections. Further study of adding the "possible acute mental status change" criterion to the revised McGeer criteria [19] for surveillance of nursing home infection appears warranted.

There has also been recent Interest regarding the role of non-localizing signs and symptoms as clinical predictors of infection in nursing home residents. The objective of a recent review was to identify specific non-localizing signs and symptoms that, when present by themselves, should result in an investigation for infection in nursing home residents[67]. After an extensive literature review, the following non-localizing signs or symptoms were identified as potential indicators of infection in nursing home residents: fever, hypothermia, hypotension, new-onset hyperglycemia, and delirium. According to the report, the findings will be used as "the foundation for an update to the Loeb minimum criteria". These recent studies [65][67] indicate that more importance is being placed on non-localizing signs and symptoms as potential predictors of infection in the elderly.

As previously noted, this review has focused on studies evaluating appropriateness of the decision-to-treat nursing home residents with suspected bacterial infection. However, there are other factors that need to be considered when assessing appropriateness of antibiotic therapy in nursing home residents including choice of antibiotic, dosing of an antibiotic in an elderly population, escalation, de-escalation, or stopping therapy, and duration of therapy. Of these factors, duration of therapy has been most extensively studied. Studies conducted in the past 20 years verify that short course treatment of pneumonia, UTI, and SSTI is effective and safe [68]. Studies in nursing home residents have identified excessively long durations of antibiotic treatment that should be a target for antibiotic stewardship programs [69][70][71].

Appropriateness of antibiotic therapy may also be influenced by non-clinical factors such as provider-, resident-, family-, and facility-level factors but there has been minimal evaluation of these issues to date. A recent study found considerable variability in facility-level rate of antibiotic use in 1,664 U.S. nursing homes[70]. Several

facility-level characteristics correlated with higher rates of antibiotic use: proportion of short-stay (≤ 100 days) residents ≥ 75%, for-profit ownership, proportion of residents with low cognitive performance scale ≥ 50%, proportion of long-stay residents with pressure ulcers ≥ 5%, and at least 1 resident on a ventilator. However, this model explained only 24% of the variability in facility-level rates of antibiotic use. Nevertheless, this study identified the importance of short-stay residents as a target for antimicrobial stewardship interventions.

Despite the limitations of the studies in this review, they can inform the development of future studies of appropriateness of antibiotic therapy in nursing home residents. First, surveillance definitions for infection should not be used for evaluating appropriateness of antibiotic therapy. Second, identification of the study population needs to be standardized, e.g., in this review, treatment with a systemic antibiotic was used in 15 studies and prescriber diagnosis of infection in 7 studies. Third, studies should be conducted prospectively. Retrospective analysis of medical records that may lack documentation of signs and symptoms of infection makes it difficult to utilize criteria dependent on these findings such as the Loeb criteria [20]. Fourth, criteria for the clinical diagnosis of common infections in the nursing home setting needs to be standardized. The planned revision of the Loeb criteria [67] may fulfill the need for standardized criteria for the clinical diagnosis of infection but will require validation studies.

In summary, although many of the studies reviewed in this paper identified low rates of appropriateness of antibiotic therapy in nursing home residents, there was considerable variation in methodology that limit interpretation and reliability of the findings. This variability indicates that the design of future studies of appropriateness of antibiotic therapy in nursing home residents needs to be standardized to improve reliability. There are also several other issues that need to be addressed. First, when evaluating appropriateness of antibiotic therapy in nursing homes, a distinction should be made between residents admitted for post-acute care and those on long-term care because the rate of antibiotic use in the post-acute population tends to be higher [70]. Second, criteria for evaluating appropriateness need to be effectively disseminated to nursing home practitioners and staff. One cannot accurately evaluate appropriateness of antibiotic prescribing using a specific set of criteria unless practitioners and staff are aware of the criteria. Lastly, further study of the association of provider-, resident-, family-, and facility-level factors with antibiotic use in nursing home residents will be important to account for these factors when assessing appropriateness of antibiotic treatment in this population.

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