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Study protocol

Optimizing antibiotics in residents of nursing homes: protocol of a randomized trial

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Abstract

Background: Antibiotics are frequently prescribed for older adults who reside in long-term care facilities. A substantial proportion of antibiotic use in this setting is inappropriate. Antibiotics are often prescribed for asymptomatic bacteriuria, a condition for which randomized trials of antibiotic therapy indicate no benefit and in fact harm. This proposal describes a randomized trial of diagnostic and therapeutic algorithms to reduce the use of antibiotics in residents of long-term care facilities.

Methods: In this on-going study, 22 nursing homes have been randomized to either use of algorithms (11 nursing homes) or to usual practise (11 nursing homes). The algorithms describe signs and symptoms for which it would be appropriate to send urine cultures or to prescribe antibiotics. The algorithms are introduced by inservicing nursing staff and by conducting one-on-one sessions for physicians using case-scenarios. The primary outcome of the study is courses of antibiotics per 1000 resident days. Secondary outcomes include urine cultures sent and antibiotic courses for urinary indications. Focus groups and semi-structured interviews with key informants will be used to assess the process of implementation and to identify key factors for sustainability.

Background

Antibiotic use in long-term care facilities

Antibiotics are frequently prescribed for older adults who reside in long-term care facilities (LTCFs). The reported prevalence of antibiotic use in nursing home residents ranges from 8% to 17% [1–4]. Prospective studies of antibiotic use in these facilities demonstrate that 50% to 75% of residents are exposed to at least one course of antibiotics over a one year period [5–8]. There are several important risks associated with the use of antibiotics in residents of LTCFs [9,10]. First, there is the risk of developing multi-drug antibiotic resistance with exposure to antibiotics [11–16]. Second, there is the risk of drug-related adverse effects. In a study of antibiotic use in Ontario facilities which provide chronic care, 6% of individuals developed an adverse effect [17]. Because polypharmacy in this population is common [18–20], the risk for harmful drug interactions in addition to adverse reactions to antibiotics is high [9]. Third, the increased use of antibiotics in LTCFs results in significant costs. In a study of antibiotic use in Manitoba nursing homes for example, over $257,000 was spent on antibiotics in the 1988–89 fiscal year for 1000 nursing home residents [7]. Clearly, optimizing the use of antibiotics in this population is an important quality of care priority.

Antibiotics for urinary indications

Urinary tract infections are the most common indication for prescribing antibiotics for residents in LTCFs. Urinary tract infections alone account for 30% to 56% of all prescriptions for antibiotics in that population [3,4,7,8,20]. The diagnosis of UTIs, like respiratory and other infections in residents of LTCFs, is difficult [9]. Clinical symptoms and signs in this population are often vague and non-specific. In the absence of valid diagnostic criteria, it is difficult to develop a strategy to optimize antibiotic use in the institutionalized elderly. Asymptomatic bacteriuria, or the presence of bacteria in the urine in the absence of urinary symptoms, is however an important exception. This condition occurs in up to 50% of older institutionalized women and 35% of institutionalized older men [21–27]. It is important to note that the term "asymptomatic" includes bacteriuria in the presence of non-specific, *non-urinary* symptoms (e.g. malaise, fatigue, functional change) [28]. It is recommended that asymptomatic bacteriuria be treated in populations at high risk of developing subsequent infection, such as children or pregnant women. However, there is compelling evidence to support not treating asymptomatic bacteriuria in residents of long-term care facilities. Data from four randomized controlled trials demonstrate a lack of benefit from treating asymptomatic bacteriuria [23,24,26,28]. These trials, conducted in part to validate the finding of an association between asymptomatic bacteriuria and death, found no effect of antibiotic treatment on mortality [29].

Despite clear evidence that supports not treating asymptomatic bacteriuria, institutionalized older adults are frequently treated for it with antibiotics. It is estimated that about one third of all prescriptions for urinary indications in nursing homes are for asymptomatic bacteriuria [3]. In a 12-month antibiotic utilization in chronic care study, 30% of prescriptions for a urinary indication were for asymptomatic bacteriuria [17].

Defining "appropriate" antibiotic use for most bacterial infections is plagued with difficulty due to diagnostic uncertainties. However, antibiotic prescribing for urinary indications is an important exception. Reducing inappropriate antibiotic use for urinary indications may be an important tactic for optimizing the use of antibiotics in LTCFs.

Qualitative study on asymptomatic bacteriuria

To help identify strategies for improving the management of asymptomatic bacteriuria in older adults in residential LTCFs, a qualitative study on reasons why antibiotics are prescribed for this condition was conducted [30]. This study revealed that ordering urine cultures and prescribing antibiotics for asymptomatic bacteriuria are largely driven by nonspecific, non-urinary symptoms (e.g. malaise, confusion, agitation). Nurses, who order urine cultures and influence physicians decision to prescribe antibiotics, were key in this process. Education and guidelines for management of asymptomatic bacteriuria and urinary tract infection were viewed by study respondents as an important priority for both physicians and nurses. Some evidence exists to suggest that systematic practise-based interventions are effective in changing physician performance [31]. Therefore, based on the best clinical evidence and our own qualitative data, we have constructed clinical algorithms for managing UTIs in older adults in LTCFs.

This paper describes the protocol of an on-going randomized trial to optimize antibiotic use in residents of nursing homes using clinical algorithms.

Methods

The primary aim of this study is to determine if an evidence-based clinical algorithm for managing urinary tract infections (UTIs) in older adults in residential long-term care facilities (LTCFs) can reduce the overall use of antibiotics in LTCFs. Secondary study questions include: Does the use of a diagnostic algorithm reduce the number of urine cultures ordered for residents in LTCFs without urinary symptoms? Does the use of a treatment algorithm reduce the number of antibiotic courses prescribed for presumptive UTIs in the target population?

Study population

Twenty-two pairs of nursing homes have been enrolled. Only free standing, community-based residential LTCFs are eligible. Other eligibility criteria include the following: 1) the facility has 100 or more residents; 2) the LTCF does not have a stated policy for diagnosis or treatment of urinary tract infections; 3) the LTCF agrees to refrain from introducing new management strategies for antibiotic utilization or clinical pathways for urinary tract infection during the study. To enhance representation for residential LTCFs in the community, the study will be limited to LTCFs not directly associated with tertiary care centres.

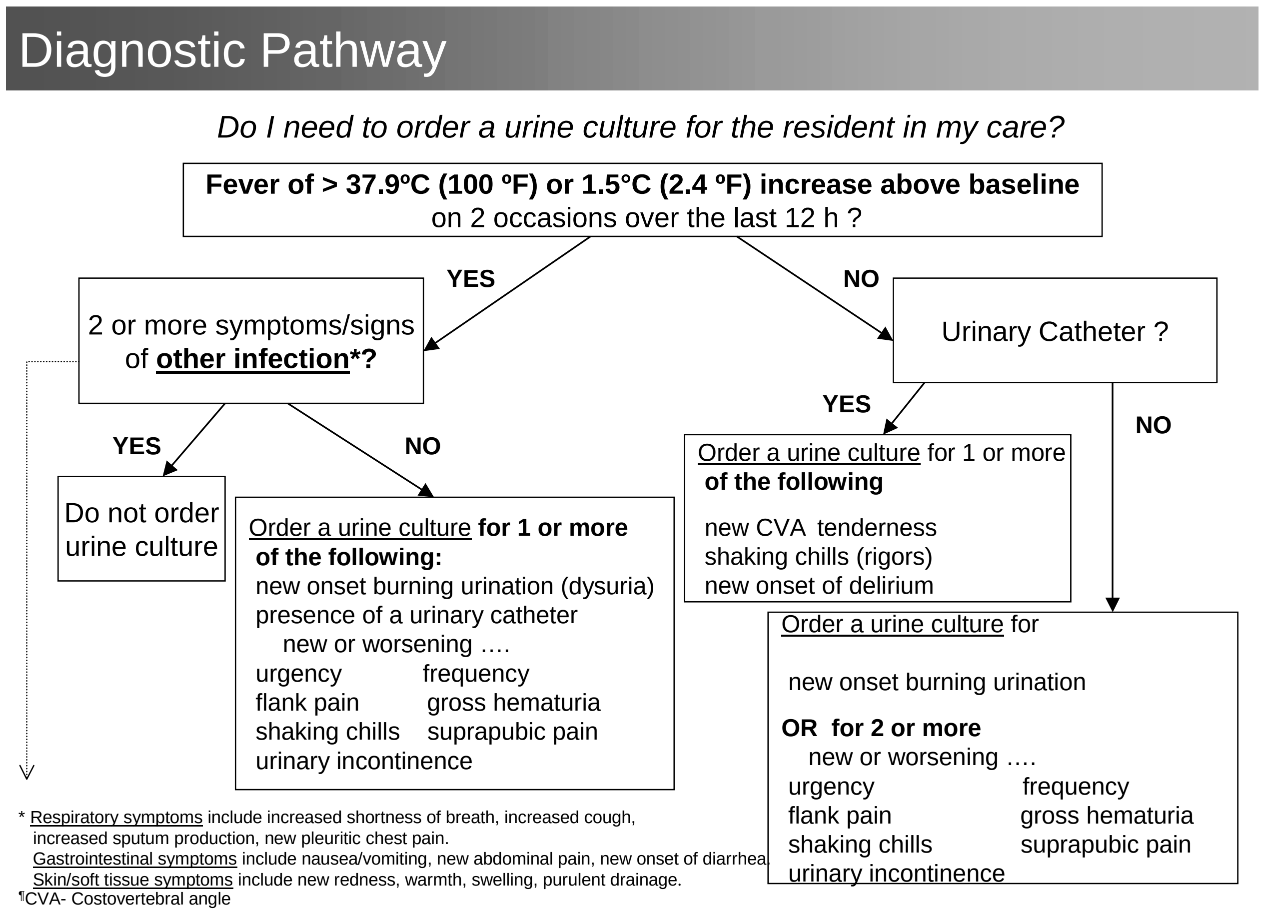

Figure 1
Diagnostic algorithm. This algorithm guides physicians and nurses in the ordering of urine cultures for nursing home residents with suspected infections.

The design is randomized matched pairs (Figure 1). Within each of the 11 pairs of LTCFs, one was randomized to the intervention (clinical algorithm), the other half to "usual" management. Quantitative outcomes will include 1) the proportion of antibiotic courses prescribed for urinary indications, 2) the total number of courses of antibiotics used, 3) rates of urine cultures ordered, 4) hospitalization rates for urinary tract infections, and 5) mortality rates. Within a LTCF, randomization of individual healthcare providers or residents to the algorithm likely would introduce bias due to contamination. Therefore, for the quantitative component of this study, the nursing home will serve as the unit of allocation and analysis.

Intervention: an evidence-based clinical algorithm

Although treatment guidelines for infections are abundant in the literature (e.g community-acquired pneumonia) few diagnostic or treatment algorithms for infections have been systematically evaluated for outcome [32,33]. A management algorithm for UTIs in nursing homes has been proposed [34]. However, no algorithms for optimizing antimicrobial use or for managing infections have been evaluated in LTCFs. Nursing staff (RNs and RPNs) play a critical role in the clinical management of LTCF residents. Physicians spend relatively little time at the bedside in LTCFs, and must rely heavily on nursing assessments. Therefore, an intervention to change clinical practise in LTCFs ideally must 1) be evidence-based, 2) be feasible to implement, 3) be inexpensive, 4) involve both nurses and physicians, 5) have the potential for strong "buy-in" from both physicians and nurses, and 6) be evaluable in terms of outcomes. We believe that our clinical algorithm for the diagnosis and treatment of UTIs in residents of LTCFs will meet these criteria.

A draft diagnostic and a treatment algorithm was developed using the best evidence available, augmented with feedback from primary care physicians and nurses work-

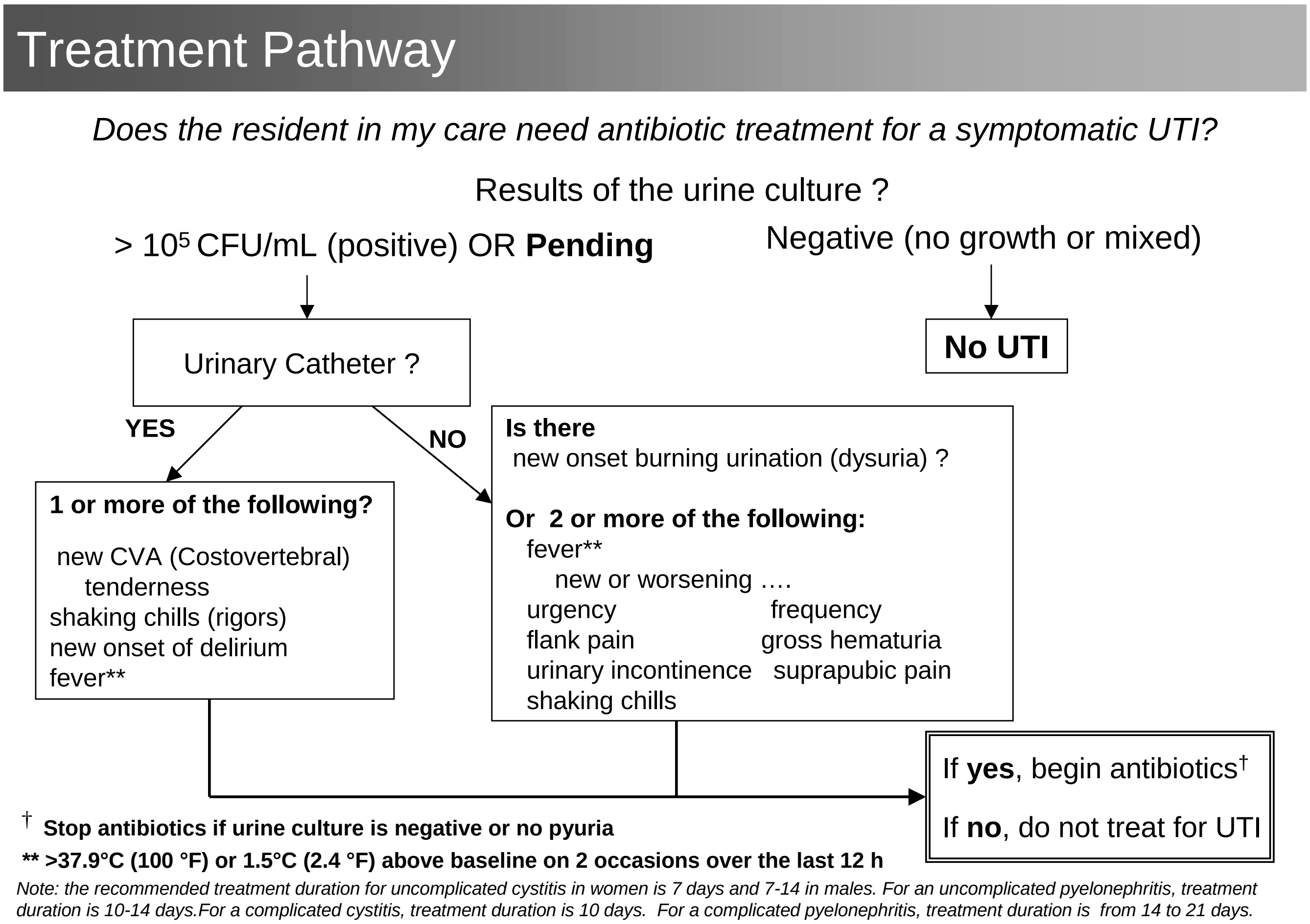

Figure 2
Treatment algorithm. This algorithm allows physicians and nurses to optimize antibiotic use in residents with suspected infections.

ing in residential LTCFs (Figure 1 + 2). Since there is no treatment benefit for asymptomatic bacteriuria [23,24,26,28], the algorithms indicate that urine should not be cultured in the absence of fever or urinary symptoms, nor should antibiotics be prescribed for positive cultures. In the absence of any urinary symptoms, only 10% of LTCF residents with fever and bacteriuria actually have a urinary infection (positive predictive value of urine culture for urinary infection in the setting of fever is 17%) (35). Therefore, prior to ordering a culture other common infections (respiratory or skin and soft tissue) need to be ruled out. When urinary symptoms are present (in the setting of bacteriuria and fever), about 50% of episodes are, serologically, urinary infections. Clinical evaluation for other infections should therefore also be conducted in such instances prior to instituting antibiotic therapy. A negative urine culture effectively rules out a urinary infection (so long as previous antibiotics were not prescribed). Although bacteriuria in the setting of pyuria is often interpreted as a "true infection", studies have shown that over 90% of the institutionalized elderly with bacteriuria also have pyuria [36,37]. Therefore the presence of pyuria and bacteriuria is not helpful. However, the absence of pyuria suggests the absence of a host response (i.e. absence of infection), therefore bacteriuria in the absence of pyuria indicates that a urinary tract infection is unlikely [29]. Gross hematuria in the institutionalized elderly generally represents an underlying structural abnormality in the genitourinary tract. About 70% of individuals with gross hematuria also have bacteriuria [38]. Since as many as 25% of individuals who develop hematuria subsequently become febrile [38], treatment of the resident with fever, gross hematuria and bacteriuria is necessary due to secondary invasive infection [39]. Since there is no relationship between the presence or absence of bacteriuria and non-urinary symptoms [28], only urinary symptoms will be assessed in the diagnostic or treatment algorithm.

Adoption of the algorithms

The algorithms were pilot-tested in four nursing homes prior to the start of the actual trial. For the trial, adoption of the intervention has been through in-services with physicians and nursing staff using case-scenarios to explain the use of the algorithms. The algorithms were printed on pocket cards and distributed to physicians and nursing staff at the start of the study. The algorithms are also kept at all nursing stations using large posters. On-site visits are planned to help with adherence to the protocol.

Data collection

Demographics of the residents and features about the facilities will be collected. Other data include the name and dose of the antibiotic, route of administration, start and stop date, reason for the prescription, as well as urinary symptoms leading to the prescription, whether a urine culture was ordered, and if so, its result. Information on deaths, all cause hospitalizations, and hospitalizations for urinary sepsis is being collected.

Analysis

The unit of analysis for this study is the nursing home. A paired t-test will be used to analyse the within-pair differences between the proportions of antibiotics prescribed for urinary indications in matched pairs of nursing homes. In this way, the fact that the denominator of the proportions is also an outcome is taken into consideration. Differences in rates of overall antibiotic use (antibiotic courses per 1000 resident days) will be compared using a paired t-test. Rates of antibiotic use for urinary indications (antibiotic courses per 1000 resident days and defined daily dosages/1000 resident days), rates of urine cultures obtained (urine cultures per 1000 resident days), rates of hospitalization (per 1000 resident days), and overall mortality rates will be compared using paired t-tests and Wilcoxon signed rank tests. Logistic regression analysis is planned to account for potentially important co-variates such as proportion of residents bed/wheelchair bound and pharmacy automatic stop dates [40].

Sample size calculation

In our 12 month study of antibiotic utilization in Ontario long-term care facilities, 30% of all antibiotic prescriptions were for urinary indications, of which one third were for asymptomatic bacteriuria. We believe that the algorithm will lead to at least a 20% reduction in the overall use of antibiotics, that is, a reduction in the proportion of antibiotic prescriptions for urinary indications from 30% to 10%. To detect this difference, for an alpha of 0.05 and 80% power, a total of 142 prescriptions (71 in each arm) is needed. To adjust for the effect of within cluster dependency, the intracluster correlation coefficient (between home variance for urinary antibiotic prescription / sum of inter- and intra-home variance), was then calculated using data from the 12 month study in Ontario long-term care facilities. The proportion of antibiotics prescribed for a urinary indication was 0.32 (p) and the variance 0.009 (between home variance). The intra-home variance, given by the binomial distribution [(p) (1-p)], was 0.21. Therefore, the intracluster correlation coefficient is 0.04. Donner et al. (41) describe a variance inflation factor given by $1 + (n - 1)\ \tau$, where τ is the intracluster correlation coefficient, and n= samples (prescriptions) needed per cluster. Since 23 prescriptions can be obtained per home per month (based on the average LTCF in our Canada-US study), and if data collection is conducted over 11 months, then n = 253. Using the formula given above, the variance inflation factor is 11. Therefore, 1562 (142×11) urinary prescriptions are required. Since these represent 30% of antibiotic prescriptions, 5206 prescriptions need to be collected in total. This means that 20 or 10 pairs of nursing homes will need to be followed for 12 months. Since matching, which would improve efficiency, was not accounted for in the sample size calculation, these figures are a conservative estimate. We will recruit another two homes to maintain the target sample size in case a pair of homes withdraws from the study.

Qualitative component

To evaluate the process of adopting the proposed algorithms in LTCFs, we plan to conduct focus groups and semi-structured interviews. Two groups of respondents will be interviewed, key clinical administrators in the participating LTCFs (medical directors, directors of nursing, infection control officers), and staff who will implement the algorithms (RN and RPN). Standard methods to ensure that the qualitative data are gathered and analyzed rigorously will be followed throughout the study. These include member checking (asking respondents to review our findings), peer review (asking colleagues to review our research process), and an audit trail (creating documents which outline all decisions made throughout the investigation) [42]. Each of these steps will be taken in this study to ensure that this portion of the study is rigorous and findings are trustworthy.

Competing interests

None declared.

Authors' contributions

All authors contributed to the development of the protocol of this randomized trial. Mark Loeb wrote the original draft of this paper and all authors offered critical revisions.

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References
1. Setia U, Serventi I, Lorenz P: **Nosocomial infections among patients in a long-term care facility: spectrum, prevalence, and risk factors.** *Am J Infect Control* 1985, **13**:57-62
2. Franson TR, Duthie EH, Cooper JE: **Prevalence survey of infections and their predisposing factors at a hospital-based nursing home care unit.** *J Am Geriatr Soc* 1986, **34**:95-100
3. Warren JW, Palumbo FB, Fitterman L, Speedie SM: **Incidence and characteristics of antibiotic use in aged nursing home patients.** *J Am Geriatr Soc* 1991, **39**:963-972
4. Zimmer JG, Bentley DW, Valenti WM, Wilson NM: **Systemic antibiotic use in nursing homes.** *J Am Geriatr Soc* 1986, **34**:703-710
5. Jacobson C, Strausbaugh L: **Incidence and impact of infection in a nursing home care unit.** *Am J Infect Control* 1990, **18**:151-159
6. Lee YL, Trupp LD, Lee R, Nothvogel S, Farsad N, Ceraio T: **Infection surveillance and antibiotic utilization in a community-based skilled nursing facility.** *Aging Clin Exp Res* 1996, **8**:113-122
7. Montgomery P, Semenchuk M, Nicolle LE: **Antimicrobial use in nursing homes in Manitoba.** *J Ger Drug Ther* 1995, **9**:55-74
8. Mylotte J: **Measuring antibiotic use in a long-term care facility.** *Am J Infect Control* 1996, **24**:174-9
9. Nicolle LE, Bentley D, Garibaldi R, Neuhaus E, Smith P: **Antimicrobial use in long-term-care facilities.** *Infect Control Hosp Epidemiol* 1996, **17**:119-128
10. Strausbaugh LJ, Crossley KB, Nurse BA, Thrupp LD: **Antimicrobial resistance in long-term-care facilities.** *Infect Control Hosp Epidemiol* 1996, **17**:129-140
11. Gaynes RP, Weinstein RA, Chambeflain W, Kabins SA: **Antibiotic-resistant flora in nursing home patients admitted to the hospital.** *Arch Intern Med* 1985, **145**:1804-1807
12. Zervos MJ, Terpenning MS, Schaberg DR, Therasse PM, Medendorp SV, Kauffman CA: **High-level aminoglycoside-resistant enterococci colonization of nursing home and acute care hospital patients.** *Arch Intern Med* 1987, **147**:1591-1594
13. Thomas JC, Bridge J, Waterman S, Vogt J, Kilman L, Hancock G: **Transmission and control of methicillin-resistant Staphylococcus aureus in a skilled nursing facility.** *Infect Control Hosp Epidemiol* 1989, **10**:106-110
14. Muder RR, Brennen C, Goetz AM, Wagener MM, Rihs JD: **Association with prior flouroquinolone therapy of widespread ciprofloxacin resistance among gram-negative isolates in a Veterans Affairs medical center.** *Antimicrob Agents Chemother* 1991, **35**:256-258
15. Muder RR, Brennen C, Drenning SD, Stout JE, Wagener MM: **Multiple antibiotic-resist gram-negative bacilli in a long-term-care facility: a case-control study of patient risk factors and prior antibiotic use.** *Infect Control Hosp Epidemiol* 1997, **18**:809-13
16. Wiener J, Quinn JP, Bradford PA, Goering RV, Nathan C, Bush K, Weinstein RA: **Multiple antibiotic-resistant klesiella and escherichia coli in nursing homes.** *JAMA* 1999, **281**:517-523
17. Loeb M, Simor A, Landry L, Walter S, McArthur M, Duffy J, Kwan D, McGeer A: **Antibiotic use in facilities which provide chronic care.** *Journal of General Internal Medicine* 2001, **16**:376-383
18. Wayne SJ, Rhyne RL, Stratton M: **Longitudinal prescribing patterns in a nursing home population.** *J Am Geriatr Soc* 1992, **40**:53-56
19. Brodrick E: **Prescribing patterns for nursing home residents in the US.** *Drugs and Aging* 1997, **11**:255-260
20. Katz PR, Beam D, Garibaldi R, Neuhaus E, Smith P: **Antimicrobial use in long-term care facilities.** *Arch Intern Med* 1990, **150**:1465-1468
21. Abrutyn E, Mossey J, Levinson M, Boscia J, Pitsakis P, Kaye D: **Epidemiology of asymptomatic bacteriuria in elderly women.** *J Am Geriatr Soc* 1991, **39**:388-393
22. Kasviki-Charvati P, Drolette-Kefakis B, Papanayiotou PC, Dontas AS: **Turnover of bacteriuria in old age.** *Age Aging* 1982, **11**:169-174
23. Nicolle LE, Bjornson J, Harding GKM, MacDonell J: **Bacteriuria in elderly institutionalized men.** *N Engl J Med* 1983, **309**:1420-1425
24. Nicolle LE, Mayhew JW, Bryan L: **Prospective randomized comparison of therapy and no therapy for asymptomatic bacteriuria in institutionalized women.** *Am J Med* 1987, **83**:27-33
25. Mou TW, Siroty R, Ventry P: **Bacteriuria in elderly chronically ill patient.** *J Am Geriatr Soc* 1962, **10**:170-175
26. Ouslander JG, Schapira M, Schnelle JF, Uman G, Fingold S, Tuico E, Nigam JG: **Does eradicating bacteriuria affect the severity of chronic urinary incontinence in nursing home residents?** *Ann Intern Med* 1995, **122**:749-754
27. Boscia JA, Kobasa WD, Abrutyn E, Levison ME, Kaplan AM, Kaye D: **Lack of association between bacteriuria and symptoms in the elderly.** *Am J Med* 1986, **81**:979-982
28. Abrutyn E, Mossey J, Berlin JA, Boscia J, Levison M, Pitsakis P, Kaye D: **Does asymptomatic bacteriuria predict mortality and does anitmicrobial treatment reduce mortality in elderly ambulatory women.** *Ann Intern Med* 1994, **120**:827
29. Nicolle LE: **Asymptomatic bacteriuria in the elderly.** *Infect Dis Clin NA* 1997, **11**:647-662
30. Walker S, McGeer A, Simor A, Armstrong-Evans M, Loeb M: **Why are antibiotics prescribed for asymptomatic bacteriuria in the institutionalized elderly? A qualitative study of physicians' and nurses' pereceptions.** *Canadian Medical Association Journal* 2000, **163**:273-7
31. Davis DA, Thomson MA, Oxman AD, Haynes RB: **Changing physician performance. A systematic review of the effect of continuing medical education strategies.** *JAMA* 1995, **274**:700-5
32. Fine MJ, Stone RA, Singer DE, Coley CM, Marrie TJ, Lave JR, Hough LJ, Obrosky DS, Schulz R, Ricci EM, Rogers JC, Kapoor WN: **Processes and outcomes of care for patients with community-acquired pneumonia: results from the Pneumonia Patient Outcomes Research Team (PORT) cohort study.** *Arch Intern Med* 1999, **159**:970-80
33. Cappelletty DM: **Critical pathways or treatment algorithms in infectious disease: do they really work?** *Pharmacotherapy* 1999, **19**:672-674
34. Beier MT: **Management of urinary tract infections in the nursing home elderly: a proposed algorithmic approach.** *Inter J Antimicro Agents* 1999, **11**:275-284
35. Orr PH, Nicolle LE, Duckworth H, Brunka J, Kennedy J, Murray D, Harding GK: **Febrile urinary infection in the institutionalized elderly.** *Am J Med* 1996, **100**:71-77
36. Nicolle LE, Ujack E, Brunka J, Bryan LE: **Immunoblot analysis of serologic response to outer membrane proteins of Escherichia coli in elderly individuals with urinary tract infections.** *J Clin Micro* 1988, **26**:1115-9
37. Rodgers K, Nicolle LE, McIntyre M, Harding GKM, Hoban D, Murray D: **Pyuria in institutionalized elderly subjects.** *Can J Infec Dis* 1991, **2**:142-146
38. Nicolle LE, Orr P, Duckworth H, Brunka J, Kennedy J, Murray D, Harding GK: **Gross hematuria in residents of long-term-care facilities.** *Am J Med* 1993, **94**:611-618
39. Nicolle LE: **Urinary infections in the elderly: symptomatic or asymptomatic.** *Inter J Antimicrobiol Agents* 1999, **11**:265-8
40. Liang KY, Zeger SL: **Longitudinal data analysis using generalized linear models.** *Biometrika* 1986, **73**:13-22
41. Donner A: **A regression approach to the analysis of data arising from cluster randomization.** *Int J Epidemiol* 1985, **14**:322-6
42. Miles MB, Huberman AM: **Qualitative Data Analysis: A Source of New Methods (2nd ed.)** *Beverly Hills, Sage* 1984

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