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American Journal of Infection Control 47 (2019) 911–915

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major article

Optimizing treatment of respiratory tract infections in nursing homes: Nurse-initiated polymerase chain reaction testing

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Key Words:
Nursing home
Pneumonia
PCR
Antibiotics
Antimicrobial stewardship

Background: Diagnostic testing using polymerase chain reaction (PCR) is infrequently initiated for diagnosis of respiratory tract infections (RTIs) in nursing homes. The objectives of this study were to determine the feasibility of implementing nurse-initiated PCR testing of respiratory specimens in nursing home settings and to compare antibiotic prescribing prior to and during the implementation.

Methods: This was a pragmatic, historically controlled study in 3 nursing homes (181 total beds) in Melbourne, Australia.

Results: The number of PCR tests of respiratory specimens (over 12 months) increased from 5 to 67 when nurses could initiate the tests. Residents with RTI symptoms had a virus identified by PCR in 50.7% of tests, including 14 positive for influenza. Six outbreaks were identified. When clustering was taken into consideration, incidence rates of antibiotic days of therapy did not change (incidence rate ratio = 0.94, 95% confidence interval, 0.25-3.35, $P = .92$) despite identification of more viral pathogens.

Conclusions: In nursing homes, nurse-initiated PCR testing of respiratory specimens is feasible and useful in terms of identifying the cause of many RTIs and outbreaks, and viruses are common in this context. However, the current study suggests the availability of these test results alone does not impact antibiotic prescribing.

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In 2017, respiratory tract infection (RTI) was the most common symptomatic indication documented for antibiotic use in the aged care National Antimicrobial Prescribing Survey of Australian nursing homes.[1] In most cases, lower RTI and pneumonia in nursing home residents are assumed to be caused by bacterial pathogens and are treated with antibiotics. However, influenza, respiratory syncytial virus, human metapneumovirus, parainfluenza viruses, coronaviruses, adenoviruses, and possibly rhinoviruses can all cause serious lower RTIs in older adults.[2-5] A 2013 study of pneumonia in hospitalized nursing home residents identified 50 viruses in 108 episodes of pneumonia.[6] Despite these findings, to date, there have been no etiologic studies using sophisticated techniques such as nucleic acid amplification (ie, polymerase chain reaction [PCR]) testing in

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Funding/support: The National Centre for Antimicrobial Stewardship and its research are funded by the National Health and Medical Research Council of Australia (APP1079625). L.D. receives an Australian Government Research Training Program Scholarship. D.C.M.K. has sat on advisory boards for Becton Dickinson Pty and MSD and received financial/travel support from MSD, all unrelated to the current work.
Conflicts of interest: None to report.
Ethics approval and consent to participate: This study was approved by a health service low-risk human research ethics committee (HREC) and registered with a university's HREC. A waiver of written consent was obtained from the HREC.

https://doi.org/10.1016/j.ajic.2019.02.001
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residents with RTI who may be safely treated in nursing home settings by general practitioners (GPs) and nurses.

Antibiotics may be beneficial for bacterial infections but are unlikely to provide any benefit to nursing home residents with viral infections. The identification of respiratory viruses can also, in many instances, allow for the cessation of unnecessary antibiotics and trigger appropriate infection prevention measures. Thus, tools to assist with accurate diagnosis of pathogens might be expected to impact antimicrobial prescribing (both antibiotic and antiviral) in nursing homes.

Inappropriate antibiotic prescribing is a well-recognized phenomenon in nursing homes[7,8] that may harm residents and lead to the development of antibiotic resistance.[9-14] The prevalence of antibiotic use in nursing homes is high.[1,15,16] Antimicrobial stewardship (AMS) activities targeting antibiotic prescribing for RTIs in this setting have, to date, been largely unexplored. Recent guidelines for AMS in long-term care facilities from the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America promote the need to design AMS activities to impact on prescribing for specific infections, such as RTIs.[17]

PCR testing of respiratory specimens can be utilized to test for the presence of viral and bacterial RTI pathogens, when clinically indicated.[18] In Australia, PCR tests performed on nose and throat specimens are recommended by *Therapeutic guidelines: antibiotic*[19] for the assessment of community-acquired pneumonia in adults and pneumonia in residents of high-level care nursing homes and in the presence of influenza-like illness. Evidence suggests that, for RTIs, investigations such as PCR testing are infrequently initiated by GPs who provide services to Australian nursing homes.[20] As such, it is important to encourage testing for suspected RTI pathogens prior to prescribing antibiotics. Empowering the nursing workforce to recognize when respiratory testing is appropriate and to initiate specimen collection may be an efficient mechanism in nursing homes when off-site GPs are unavailable or do not have responsibility for infection prevention oversight. Nurses have a pivotal role in AMS in nursing homes.[21] The objectives of this study were to determine the feasibility of implementing nurse-initiated PCR testing of respiratory specimens in nursing home settings and to compare antibiotic prescribing prior to and during implementation.

METHODS

This was a pragmatic, historically controlled study.[22] It was undertaken in 3 nursing homes affiliated with a metropolitan health care service in Melbourne, Australia: a 100-bed home serviced by 3 regular GPs, a 46-bed home serviced by 2 regular GPs, and a 35-bed home serviced by 1 regular GP. All GPs had consulting rooms offsite and visited their respective nursing homes regularly 1 day each week. Each nursing home had 1 registered nurse (RN) facility manager and 1 or 2 RNs available on all shifts for resident care. Other regular staff in each home included part-time RN infection control nurse consultants, enrolled nurses, and personal care assistants. Locum GPs and nurse and personal care assistant bank staff were commonly utilized by the homes during the study. There were no changes to GP or pharmacy services during the 24-month duration of this study, but a new director of nursing overseeing all sites and a new RN facility manager started employment at the 100-bed home just prior to the start of the intervention period.

Preintervention

The preintervention data collection period spanned 12 months, from August 2015 to July 2016, at the 46- and 35-bed homes and 12 months, from October 2015 to September 2016, at the 100-bed home. Prior to the intervention, when a resident became unwell with respiratory symptoms and could safely be treated in the nursing home, the resident's GP would be notified by the nursing home staff and the GP would advise over the telephone or attend to the resident when available. If the resident's usual GP was unavailable, an after-hours locum GP would be organized to visit the resident if deemed necessary by the nursing home staff. A routine infection register with associated antibiotic prescribing was maintained in each home, started by the nursing staff when a resident became unwell, and completed and monitored by the infection control nurse consultants.

Intervention

The intervention was conducted over 12 months, from August 2016 to July 2017, at the 46- and 35-bed homes and over 12 months, from October 2016 to September 2017, at the 100-bed home. In the weeks prior to the intervention period, the nursing home nurses and GPs were provided with education (written handouts for the GPs and an education session with an infection control nurse consultant for the nurses) with regard to following practices as described in *Therapeutic guidelines: antibiotic*,[19] in which they were to consider the use of PCR testing of respiratory specimens for residents with new-onset clinical signs or symptoms of RTI whenever they were considering the need for an antibiotic to treat an RTI or whenever there was a suspected influenza-like illness or outbreak. The usual care relationships and systems at each participating nursing home to identify and treat residents who were unwell were maintained (eg, family members were notified and asked to verbally consent if that was the usual practice for an unwell resident). The nursing home was asked to notify the resident's GP when a respiratory specimen was collected for PCR testing. An investigator (L.D.) met with the nurses, GPs, other staff, residents, and family members from the nursing homes to explain the study and distribute information materials about the intervention. The infection control nurse consultants conducted education sessions with staff from the homes, including education for nurses regarding the collection of respiratory specimens (from the nasopharynx) using flocked swabs.

Standing orders for PCR testing of respiratory specimens were introduced into the nursing homes to enable the nurses to initiate the testing. The nurses were trained to collect and store the specimens as per the swab manufacturer's instructions. Prefilled pathology request forms and appropriately stored specimens were transferred by courier for testing to the health services' pathology laboratory.

Specimens were analyzed using AusDiagnostics Pty. Ltd. (Mascot, NSW, Australia) multiplex PCR run by the High-Plex system (Cat. No. 9150) and respiratory pathogen B (16-well) kit version 2 (Cat. No. 20612). Samples were analyzed for the presence of influenza A and B; parainfluenza; respiratory syncytial virus A and B; adenovirus; rhinovirus and enterovirus; human metapneumovirus; *Bordetella pertussis, Bordetella parapertussis*, and *Bordetella bronchiseptica*; *Chlamydia* and *Chlamydophila*; *Mycoplasma pneumoniae*; and *Legionella pneumophila* and *Legionella longbeachae*. When results of the PCR testing were received by the nursing homes, they were communicated to the residents' GPs via the usual practices (either telephoning the GP for urgent matters or placing the results in the resident's medical record). During the intervention, the nursing home GPs and RNs were given regular reminders from the infection control nurse consultants and study investigator (L.D.) about the intervention.

Data collection

Soon after a respiratory specimen was collected, the nursing home staff started a study case record form (CRF). The CRF was later completed by an investigator (L.D.) using information from the resident's medical record. If the specimen collection was refused by a resident or family member, this was indicated on a CRF. The CRF captured specimen collection details and PCR results, results of any other diagnostic tests, antibiotic and antiviral prescribing and administration details, whether the resident was clinically reviewed after the test results and when, infection outcome, demographic data, comorbidities, other ongoing infections and treatment, infection prevention precautions, and any related outbreaks in the nursing home.

Routine infection surveillance captured the number of RTI episodes, occupied bed days (OBDs), diagnostic test results, and antibiotic courses. A course of antibiotics was defined as a prescribed period of treatment with 1 antibiotic. Whether the documented signs and symptoms of the RTI episode met McGeer criteria for pneumonia or lower RTI[23] was assessed and recorded by the infection control nurse consultants from data in the resident's medical record, independent from the study investigators. These criteria were used to suggest whether the episode was more likely a lower RTI or an upper RTI. The McGeer criteria are utilized as surveillance criteria and to benchmark antibiotic prescribing in Australian nursing homes[1,20] and are not diagnostic criteria. Antibiotic days of therapy (DOT) data were collected prospectively during the intervention and retrospectively from resident records for the preintervention period by an investigator (L.D.) for all residents with RTI episodes recorded on the infection registers during the periods of investigation.

Data analysis

Data were analyzed using SPSS Statistics Version 23.0 (IBM, Armonk, NY) for Windows (Microsoft, Redmond, WA). Wilcoxon matched-pairs signed-rank tests were used to assess changes to numbers of OBDs, RTI episodes, and antibiotics prescribed per 1,000 OBDs. Also, χ^2 tests were used to analyze categorical data (RTI episodes treated with more than 1 antibiotic course and RTI episodes meeting McGeer criteria). To account for clustering of antibiotic use within the nursing homes, antibiotic prescribing was further evaluated using a Poisson regression with robust standard errors using OBDs as the offset. Missing antibiotic DOT data were excluded from the analysis.

RESULTS

Preintervention

Infection surveillance recorded 1.9 episodes of RTI per 1,000 OBDs (120 RTIs, 63,808 OBDs) in the 12 months prior to the intervention across all participating nursing homes (Table 1). Of all recorded RTI episodes, 38.3% (46 of 120) met McGeer criteria[23] for pneumonia or lower RTI. Respiratory specimens were collected for PCR testing in 4.2% (5 of 120) of RTI episodes recorded in the preintervention period. One was positive for influenza B, and no pathogens were detected in the 4 other samples. No RTI outbreaks were identified. One hundred and thirty-two antibiotic courses (Table 2) were recorded for 120 RTI episodes. Eighteen RTI episodes were treated with more than 1 course of antibiotics. Thirteen RTI episodes were not treated with antibiotics. Missing medical records resulted in antibiotic DOT data from 21 courses being excluded from the preintervention data collection.

Table 2
Antibiotics prescribed

Antibiotic courses prescribed for RTIs	12 months preintervention	12-month intervention
Amoxicillin + clavulanic acid	40	45
Amoxicillin	30	29
Roxithromycin	29	27
Doxycycline	16	19
Cephalexin	6	7
Ceftriaxone	7	6
Ciprofloxacin	0	2
Cefuroxime	0	2
Clarithromycin	1	1
Moxifloxacin	2	0
Erythromycin	1	0
Benzylpenicillin	0	1
Total antibiotic courses	132	139

RTIs, respiratory tract infections.

Intervention

Fifty-five nursing home residents with 72 distinct RTI episodes were identified and approached for PCR testing. Four residents were approached on 3 occasions for 3 RTI episodes, 9 residents were approached on 2 occasions for 2 RTI episodes, and 42 residents were approached on 1 occasion for 1 RTI episode. Five PCR tests were declined by 4 residents (or family members). One resident declined on 2 occasions for 2 RTI episodes, and 3 residents declined on 1 occasion. Table 3 contains the demographics, investigation results, and outcomes of the residents identified for PCR testing.

During the intervention, 2.6 episodes of RTI per 1,000 OBDs (161 RTIs, 62,251 OBDs) were recorded as part of routine infection

Table 1
Changes to OBDs, RTI episodes, and antibiotics

	12 months preintervention		12-month intervention		
	Total in all nursing homes	Mean per nursing home	Total in all nursing homes	Mean per nursing home	*p* value
RTI episodes	120	40.0	161	53.7	0.59†
RTI episodes meeting McGeer criteria for pneumonia or lower RTI	46	15.3	51	17.0	0.95‡
OBDs	63,808	21,269	62,251	20,750	0.59†
RTI episodes per 1,000 OBDs	1.9*	1.5	2.6*	2.7	0.59†
RTI episodes treated with greater than 1 antibiotic course	18	6.0	21	7.0	0.73‡
Antibiotic DOT per 1,000 OBDs	9.7*	8.5	12.9*	13.0	1.0†
Antibiotic DOT per 1,000 OBDs prescribed for RTI episodes not meeting McGeer criteria for lower RTI or pneumonia	5.8*	4.9	7.0*	6.1	0.29†
Antibiotic courses per 1,000 OBDs	2.1*	1.6	2.2*	2.3	0.59†
Antibiotic courses per 1,000 OBDs prescribed for RTI episodes not meeting McGeer criteria for lower RTI or pneumonia	1.2*	0.9	1.2*	1.0	1.0†

DOT, days of therapy; *OBDs*, occupied bed days; *RTI*, respiratory tract infection.
*Rate per 1,000 OBDs in pooled sample.
†Wilcoxon matched-pairs signed-rank test.
‡χ^2 test.

Table 3
Demographics and results of residents with RTI signs and symptoms identified for PCR testing

Demographics	N = 72*
Median age in years (range)	76 (60-91)
Male sex (%)	48 (66.7)
Comorbidities (%)	
Cognitive impairment	59 (81.9)
Depression or anxiety	41 (56.9)
Inability to ambulate independently	36 (50.0)
Coronary artery disease	29 (40.3)
Chronic respiratory disease	24 (33.3)
Diabetes	23 (31.9)
Assisted feeding	11 (15.3)
PCR results (%)	
None detected	33 (45.8)
Rhinovirus or enterovirus	20 (27.8)
Influenza A	14 (19.4)
Declined test	5 (6.9)
Other investigations (%)†	
Positive sputum microbiology	1 (1.4)
Radiographic suspicion of pneumonia	0 (0.0)
Positive blood culture	0 (0.0)
Positive urine microscopy and culture	0 (0.0)
White blood cell count suspicion of infection	0 (0.0)
Episode outcomes (%)	
Recovered in nursing home	67 (93.1)
Palliative care/died	4 (5.6)
Transferred to hospital	1 (1.4)

PCR, polymerase chain reaction; *RTI*, respiratory tract infection.
*Some residents are counted more than once.
†In most cases, these investigations were not ordered (sputum microbiology n = 2, chest radiograph n = 3, blood culture n = 3, urine microscopy and culture n = 4, white blood cell count n = 5).

surveillance across all participating nursing homes (Table 1). Of all RTI episodes recorded, 31.7% (51 of 161) met McGeer criteria[23] for pneumonia or lower RTI. Almost 45% of all RTI episodes recorded on the infection registers (72 of 161, 44.7%) were identified for the study's PCR testing. PCR tests were declined on approach on 5 occasions (5 of 72, 6.9%), leaving 67 specimens for analysis. Of the 72 RTI episodes identified for PCR testing, 19 (26.4%) met McGeer criteria[23] for lower RTI or pneumonia. The mean time to a PCR result after a specimen was collected was 1.5 days (range, same day to 5 days). Eight specimens were tested by pathology services different from the one recommended by the study protocol.

More than half of the specimens collected (34 of 67, 50.7%) were positive for a respiratory virus, and no bacteria were detected by the study's PCR testing. Rhinovirus or enterovirus were detected in 29.9% (20 of 67) of specimens, and influenza A was detected in 20.9% (14 of 67). Additionally, 2 sputum samples were collected and analyzed by standard bacterial culture, one returning "moderate growth of normal flora" in a resident who declined the study's PCR testing and the other "*Streptococcus pneumoniae*" in an RTI episode with no pathogen detected by the study's PCR testing. No other investigations (chest radiographs, blood or urine cultures, white cell count) were suggestive of infection in tested episodes. These investigations were rarely ordered (chest radiograph n = 3, blood culture n = 3, urine microscopy and culture n = 4, white cell count n = 5).

One hundred and thirty-nine antibiotic courses (Table 2) were recorded for 161 RTI episodes in the intervention period. Twenty-one RTI episodes were treated with more than 1 course of antibiotics. Forty RTI episodes were not treated with antibiotics. Antibiotics were prescribed for 37.3% (25 of 67) of the PCR-tested RTI episodes before the PCR result was available. Nine antibiotic courses continued after a positive PCR result for a virus was known. One was positive for influenza A, and 8 were positive for rhinovirus or enterovirus. Antibiotics were discontinued for 4 RTI episodes (4 of 25, 16.0%) after a virus-positive PCR test result, but only one appeared to be directly related

Table 4
Poisson regression with OBDs as the offset

	IRR (95% CI)	*P* value
Preintervention 12 months	1.00	–
Intervention 12 months		
Antibiotic DOT	0.94 (0.25-3.35)	.92
Antibiotic DOT prescribed for RTI episodes not meeting McGeer criteria for lower RTI or pneumonia	0.85 (0.32-2.27)	.74
Antibiotic courses	0.77 (0.22-2.66)	.67
Antibiotic courses prescribed for RTI episodes not meeting McGeer criteria for lower RTI or pneumonia	0.73 (0.28-1.90)	.52

CI, confidence interval; *DOT*, days of therapy; *IRR*, incidence rate ratio; *OBDs*, occupied bed days; *RTI*, respiratory tract infection.

to the test result, when treatment was switched from an antibiotic to the antiviral oseltamivir after a positive influenza result. For 2 other RTI episodes, the associated antibiotic courses were ceased before the specified completion dates because the residents were started on palliative care plans, and for 1 RTI episode, the resident was transferred out of the nursing home before antibiotic course completion.

The impact on infection prevention activities was not specifically measured, although 73.6% (53 of 72) of RTI episodes identified for the study's PCR testing had at least 1 documented infection prevention measure initiated (eg, room isolation, respiratory hygiene). During the 12-month intervention, there were 4 outbreaks of rhinovirus or enterovirus (chronologically, the outbreaks had 5, 3, 6, and 3 confirmed cases) and 2 outbreaks of influenza A (with 12 and 2 confirmed cases). The use of prophylactic antivirals for residents in contact with the influenza cases was not observed.

Preintervention vs intervention antibiotic therapy

A substantial number of antibiotics were prescribed for RTI episodes not meeting McGeer criteria for lower RTI or pneumonia (suggestive of upper RTI) both prior to and during the intervention. Prior to the intervention, 56.1% (74 of 132) of antibiotic courses and 59.7% (371 of 621) of antibiotic DOT were prescribed for RTI episodes not meeting these criteria, whereas during the intervention, 53.2% (74 of 139) of antibiotic courses and 54.3% (433 of 800) of antibiotic DOT were prescribed for RTI episodes not meeting these criteria.

Table 1 outlines the mean numbers of RTI episodes, OBDs, and associated antibiotic DOT and antibiotic courses prescribed per nursing home prior to and during the intervention. Both the mean number of RTI episodes and the number of RTI episodes treated with more than 1 antibiotic course were unchanged. Antibiotic DOT per 1,000 OBDs was unchanged after the introduction of nurse-initiated PCR testing of respiratory specimens. This was true for all antibiotics and antibiotics prescribed for RTI episodes where symptoms did not meet McGeer criteria for lower RTI or pneumonia. Similarly, antibiotic courses for RTI episodes per 1,000 OBDs were not changed by the intervention (Table 1).

Incidence rates of antibiotic prescribing also did not change when clustering of antibiotic prescribing within nursing homes was taken into consideration (Table 4). The intervention also did not appear to influence the types of antibiotics prescribed in these nursing homes, as the 6 most frequently prescribed antibiotics were unchanged (Table 2).

DISCUSSION

In this study, nurse-initiated PCR testing of respiratory specimens in nursing homes was successfully implemented as part of everyday practice. This suggests that in real-world practice, educating and empowering nursing home nurses to recognize respiratory symptoms and initiate swabbing for PCR testing can increase the number of tests within a nursing home and provide more information about circulating respiratory pathogens. This study identified a high rate of viral respiratory pathogens circulating in nursing home settings (50.7%). Despite the increase in identification of viruses through PCR, there was no change in the pattern of antibiotic prescribing.

The fact that increased viral identification did not lead to a reduction in antibiotic use is of interest. Although the protocol specified the results of the PCR testing were to be forwarded to the resident's GP, who was "offsite," the use of paper records in these nursing homes meant that information on "if and when" the GPs reviewed the results could not be documented. In some acute hospital settings, reporting similar results directly to attending physicians has also not been sufficient to change antibiotic prescribing behaviors.[24-26] In hospitals, reporting the PCR result to an AMS team along with specific advice from the AMS team about antibiotic cessation is required to impact prescribing behavior.[24] Slow transfer of information, lack of confidence in the results, and other factors within the nursing homes, such as work flow, resident mix, and prescriber preferences for overly cautious antibiotic prescribing,[27] may have affected the outcome of this study. The impact of the PCR testing might have been more significant if a clear algorithm to guide prescribers regarding how to respond to the results was in place. Prescribers might also have needed more information to improve their confidence in the validity of the results.

Nursing home residents are often clinically complex, and prescribers may be overly cautious about possible dual pathology (eg, mixed viral/bacterial infection). For some residents (eg, those with fever, cough, and a demonstrated viral pathogen), a prescriber's readiness to cease antibiotic therapy based on PCR test results may change as they become more confident with using the test.

Although not statistically significant, it may be clinically significant that the intervention was also associated with an increase in recognized episodes of RTI (1.5 vs 2.7 RTIs per 1,000 OBDs). This increase may be a true phenomenon or due to heightened recognition of symptoms and signs of RTI, leading to more reporting. Heightened recognition of RTIs in nursing homes can positively impact important infection prevention activities, such as respiratory and hand hygiene. Importantly, the PCR tests enabled outbreaks of viral pathogens to be identified, and this may have major implications in terms of enabling infection prevention strategies to limit transmission.

CONCLUSIONS

In nursing homes, the introduction of nurse-initiated PCR testing of respiratory specimens is feasible and useful in terms of identifying the cause of many respiratory illnesses and outbreaks. However, the current study suggests additional resources may be required to influence antibiotic prescribing behaviors for RTIs in nursing homes. Guidance from clinical algorithms or other support, such as input from an AMS clinician,[24] in addition to nurse-initiated PCR testing, may be required to impact antibiotic prescribing for RTIs in nursing homes.

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