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Original Study

An Electronic Health Record Integrated Decision Tool and Supportive Interventions to Improve Antibiotic Prescribing for Urinary Tract Infections in Nursing Homes: A Cluster Randomized Controlled Trial



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A B S T R A C T

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Objective: To investigate whether an electronic health record (EHR)–integrated decision tool, combined with supportive interventions, results in more appropriate antibiotic prescribing in nursing home (NH) residents with suspected urinary tract infection (UTI), without negative consequences for residents.

Design: Cluster randomized controlled trial with NHs as the randomization unit; intervention group NHs received the EHR-integrated decision tool and supportive interventions, and control group NHs provided care as usual.

Setting and Participants: 212 residents with suspected UTI, from 16 NHs in the Netherlands.

Methods: Physicians collected data at index consultation (ie, UTI suspicion) and during a 21-day follow-up period (March 2019–March 2020). Overall antibiotic prescribing data at NH level, 12 months prior to and during the study, was derived from the electronic prescribing system. The primary study outcome was the percentage of antibiotic prescriptions for suspected UTI that was appropriate, at index consultation. Secondary study outcomes included changes in treatment decision, complications, UTI-related hospitalization, and mortality during follow-up; and pre-post study changes in antibiotic prescribing at the NH level.

Results: 295 suspected UTIs were included (intervention group: 189; control group: 106). The between-group difference in appropriate antibiotic prescribing was 13% [intervention group: 62%, control group: 49%; adjusted odds ratio (OR) 1.43, 95% CI 0.57–3.62]. In both groups, complications (2% vs 3%), UTI-related hospitalization (2% vs 1%), and possible UTI-related mortality (2% vs 2%) were rare. The pre-post study difference in antibiotic prescriptions per 1000 resident-care days was -0.95 in the intervention group NHs and -0.05 in the control group NHs ($P = .02$).

Conclusion and Implications: Although appropriate antibiotic prescribing improved in the intervention group, this does not provide sufficient evidence for our multidisciplinary intervention. Despite this

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inconclusive result, our intervention could potentially still be effective, because we established a large reduction in the number of antibiotic prescriptions in the intervention group.

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Antibiotics are frequently prescribed in nursing homes (NHs), in particular for urinary tract infections (UTIs).¹ Previous research found that one-third of the antibiotic prescriptions for UTI in this setting are not appropriate.² Diagnosing UTI in NH residents is challenging for various reasons. First, several resident subgroups (eg, with dementia) are not able to report or indicate their symptoms.³ In addition, a gold standard to establish UTI in frail older adults is lacking.⁴ Furthermore, nursing staff, residents, and their family can pressure physicians to prescribe antibiotics.⁵ Taken together, as a consequence, physicians frequently prescribe antibiotics to be “better safe than sorry.”⁶

Antibiotics are often inappropriately prescribed for residents with nonspecific signs and symptoms (S&S), such as changes in behavior or mental status. Physicians regularly attribute such S&S to UTI, whereas these can be an expression of many other causes.⁷ In addition, antibiotics are frequently prescribed in response to a positive urine dipstick test. However, asymptomatic bacteriuria prevalence rates up to 52% are reported for men and up to 76% for women, which makes urinalysis unsuitable to confirm the UTI diagnosis (but only suitable to rule out this diagnosis).^{8–12}

Disadvantages of inappropriate antibiotic prescribing include side effects, drug interactions, and intestinal infections caused by *Clostridium difficile*, to which frail older adults are more susceptible.^{13,14} Further, inappropriate antibiotic use can lead to undertreatment of other conditions, if no further assessment is done to look for alternative causes that may underlie the S&S ascribed to UTI. Finally, antibiotic use is an important risk factor for the development of antibiotic resistance.¹

Considering these disadvantages, it is important to promote appropriate antibiotic prescribing. Therefore, we developed an electronic health record (EHR)–integrated decision tool, based on a previously developed decision tool for the treatment of suspected UTI in frail older adults.¹⁵ Earlier research showed that electronic decision support has the potential to improve antibiotic prescribing; however, to our best knowledge, this has not yet been investigated for the NH setting.¹⁶ Therefore, the aim of this study was to investigate whether the EHR-integrated decision tool, in combination with supportive interventions for physicians and nursing staff, results in more appropriate antibiotic prescribing in residents with suspected UTI, without negative consequences for residents.

Methods

Study Design

We conducted a cluster randomized controlled trial in 16 NHs in the Netherlands, with NHs as the unit of randomization. Six control group NHs provided care as usual. Ten intervention group NHs were provided a decision tool for the treatment of residents with suspected UTI, integrated in the EHR Ysis (Gerimedica, Amsterdam, the Netherlands). The treatment advice generated by this decision tool corresponds to the advice stated in the UTI guideline of the Dutch Association of Elderly Care Physicians (Verenso),¹⁷ which is identical to the advice in the previously mentioned decision tool that was developed in an international Delphi study (Supplementary Material 1).¹⁵ Box 1 provides a summary of those situations in which antibiotic prescribing is indicated for suspected UTI in NH residents, according to this advice.

Box 1. Situations in Which Antibiotic Prescribing Is Indicated for Suspected UTI in NH Residents, According to the Advice Generated by the Decision Tool^{15,18}

Residents without an indwelling catheter:

- More than 1 of the following S&S or 1 of these S&S if very bothersome, if accompanied by systemic S&S, or if accompanied by costovertebral angle pain/tenderness and/or suprapubic pain: recent onset of dysuria, urgency, frequency, incontinence, (visible) urethral purulence.
- Costovertebral angle pain/tenderness of recent onset, accompanied by systemic S&S.
- For both situations above: antibiotic prescribing is advised *unless* urinalysis shows negative nitrite and negative leukocyte esterase.

Residents with an indwelling catheter:

- Antibiotic prescribing is advised if there is no other infectious focus *and* at least 1 of the following: fever (≥ 24 h), rigors/shaking chills, clear-cut delirium (after excluding urinary retention as a possible cause).

The EHR-integrated decision tool was accompanied by supportive interventions for physicians (ie, an interactive training session provided by the research team, pocket-cards, and an information leaflet to hand out to residents and/or their family) and nursing staff (ie, an e-learning, a short video, pocket-cards, and an information leaflet to hand out to residents and/or their family). A more detailed description of these interventions, as well as the study design and study procedures, is provided elsewhere.¹⁸

Eligibility Criteria and Informed Consent Procedure

Inclusion criteria for NHs to participate were (1) having at least 150 beds on psychogeriatric and/or somatic departments and (2) using the EHR Ysis. Upfront, NH staff asked all residents—or their representatives in case of decisive incapacity—for consent to participate in case they would develop a possible UTI during the study period (ie, pre-emptive consent). Consenting residents with a suspected UTI were included if they had not used antibiotics in the previous 7 days, and if they did not have a recorded wish to not be treated with antibiotics in case of a UTI.

Data Collection

Physicians of the participating NHs collected data from March 2019 to March 2020 at index consultation (ie, UTI suspicion) and during a 21-day follow-up period using case report forms (CRFs) integrated in the EHR. The initial CRF appeared automatically when a physician entered “urinary tract infection” or a synonym in the EHR. The follow-up CRFs were provided 3, 7, and 21 days later in the intervention group and 7 and 21 days later in the control group.

The CRF at index consultation contained questions on S&S [specific: recent onset of dysuria, urgency, frequency, incontinence and (visible) urethral purulence; nonspecific: eg, agitation and confusion; and systemic: fever, rigors, and clear-cut delirium], diagnostics (eg, urinalysis), treatment (ie, whether antibiotics were started or not), and comorbidity (eg, dementia, urinary tract abnormalities, cardiovascular and pulmonary diseases). The follow-up CRFs contained questions on complications, UTI-related hospitalization, and

mortality. Patient characteristics such as age and gender were automatically derived from the EHR. Lastly, we collected anonymous data on total antibiotic prescriptions in the participating NHs, derived from the electronic prescribing system, from 12 months prior to study onset to study conclusion.

Outcomes

The primary study outcome was the percentage of antibiotic prescriptions for suspected UTI that were appropriate (yes/no), that is, prescribed in compliance with the treatment advice generated by the decision tool. Secondary study outcomes included changes in treatment decision (ie, antibiotic start after initial withholding antibiotics), complications (side effects of antibiotics, renal insufficiency, and pyelonephritis/urosepsis), UTI-related hospitalization, and mortality during follow-up, and pre-post study changes in total antibiotic prescribing at the NH level.

Randomization

Randomization was performed by an independent statistician by using randomization software.

Sample Size

We considered an increase of at least 20% appropriate antibiotic prescribing for suspected UTI to be clinically relevant.² To detect this difference with 80% power and a significance level of 5%, 72 cases of antibiotic prescribing for UTI would be required in each group.¹⁹ Based on previous study data,² we expected that antibiotics would be prescribed in 91% of cases of suspected UTI in the control group and that our intervention had the potential to reduce this to 62% of suspected UTI in the intervention group. Consequently, 79 cases of suspected UTI were required in the control group to include 72 antibiotic prescriptions, and up to 116 in the intervention group.

We decided to include NHs with 150 beds on average. Dutch surveillance studies reported an incidence rate of 87 UTIs per 150 beds per year.²⁰ Based on prior, comparable research,² we estimated that 70% of the residents (or their representatives in case of legal incapacity) would provide informed consent to participate in the study, which converts to 61 recruited residents per 150 beds per year for the present study.

Corrected for clustering within NHs, we needed $(79 \times 4.6=)$ 363 cases in the control group and $(116 \times 4.6=)$ 534 in the intervention group, using the following formula for design effect: $1 + [(cluster\ size - 1) \times intraclass\ correlation\ coefficient] = 1 + [(61 - 1) \times 0.06] = 4.6$. The estimate of the intraclass correlation coefficient was based on Campbell et al and prior study data.^{2,21} To include 363 cases over a period of 12 months, 6 NHs (ie, 363/61) were required in the control group. To include 534 cases over a period of 12 months, 9 NHs (ie, 534/61) were required in the intervention group.

Statistical Analysis

We used independent *t* test for continuous variables and chi-square tests for categorical variables to compare characteristics of the study population.

The primary analyses assessed the difference between the intervention and the control group in the percentage of antibiotic prescriptions for suspected UTI that were appropriate, at index consultation. First, we performed an intention-to-treat analysis. Second, we performed 2 subgroup analyses of patients in which applicability of the interventions may potentially be reduced: patients with (very) severe dementia, and patients with urine incontinence. Finally,

we performed analyses with an interaction term to establish whether there was a significant difference in effect for these subgroups.

For the above-mentioned analyses, we used generalized estimating equations (GEEs). Prior to this analysis, we investigated whether there was correlation of the data within the different clusters (1: at resident level, 2: at prescriber level, 3: at NH level) by testing the ICC with the likelihood ratio test. A significant ICC was only found at prescriber level. Because we had too few cases to correct for all possible confounders, we used the forward confounder selection method to assess which confounders influenced the odds ratio (OR) most.²² This resulted in correction for gender, pulmonary diseases, (very) severe dementia, indwelling catheter, consultation during evenings/weekend, and mean number of antibiotic prescriptions per 1000 resident-care days on the NH level in the 12 months prior to study onset.

The secondary analyses assessed the difference between residents with suspected UTI in the intervention and the control group, with regard to changes in treatment decision, complications, UTI-related hospitalization, and mortality during 21-day follow-up. For these analyses, we anticipated to use the above-described GEE analyses. However, because there were too few cases for GEE analyses, we decided to perform descriptive analyses.

In order to describe the potential impact of adjusted antibiotic prescribing for UTI on overall and UTI-related (defined as nitrofurantoin, fosfomycin, and trimethoprim, as these drugs are exclusive for treatment of UTI in the Netherlands) antibiotic prescribing, we plotted the total prescriptions per 1000 resident-care days per month for both the intervention and control group. To assess whether the pre-post study differences in the number of (UTI-related) antibiotic prescriptions per 1000 resident-care days were significantly different between the intervention and control group, we performed independent *t* test analyses. We excluded prophylactic prescriptions and chronic prescriptions (>42 days).

GEE analyses were performed using Stata, version SE 14 (StataCorp, LLC), other analyses were performed using SPSS, version 20.0 (IBM Corp).

Ethics

The Medical Research Ethics Committee of the Amsterdam University Medical Centers, location VU University Medical Center, approved our study protocol on December 27, 2018. On February 26, 2019, we registered our study in the Netherlands Trial Register under number NL7555. Written informed consent was obtained from all study participants or their representatives.

Results

Recruitment and Participant Characteristics

Sixteen NHs located across west, central, and southeast Netherlands participated in the study. During the study, an average of 2697 residents resided on the participating wards (intervention group: 1649; control group 1048) (Figure 1). All residents were asked for study participation in case they would develop a suspected UTI during the study period. A total of 693 of these 2697 residents provided informed consent [intervention group: 409 (25%); control group 284 (27%)]. In these 693 residents, a UTI was suspected 345 times. Among the 345 UTI suspicions, 295 were eligible for inclusion (intervention group: 189, control group: 106), 24 were excluded because of (recent) antibiotic use [intervention group: 18 (8%); control group 6 (5%)] and 19 did not wish to be treated with antibiotics in case of UTI [intervention group: 14 (6%); control group: 5 (4%)]. In the intervention group, 114 of the 189 cases (60%) were treated with

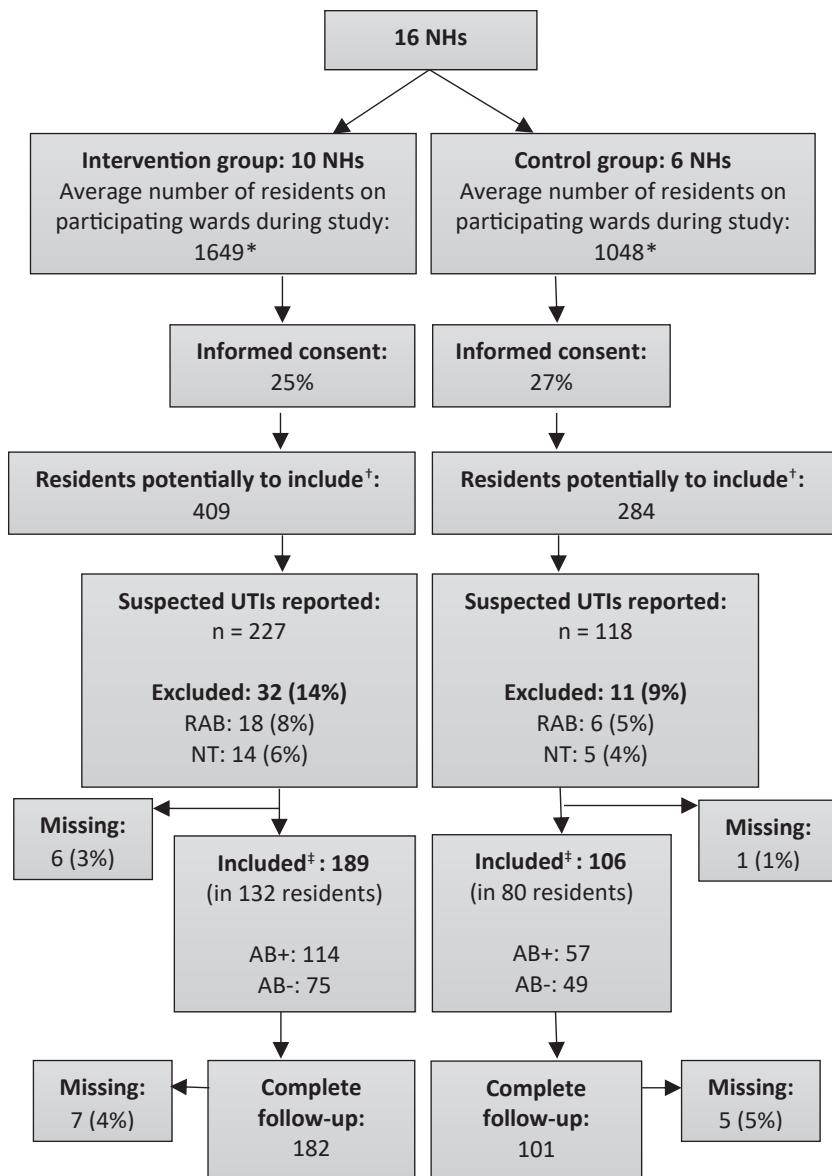


Fig. 1. Study flowchart. AB+, treated with antibiotics; AB-, not treated with antibiotics; NT, residents who do not wish to be treated with antibiotics in case of UTI; RAB, residents with (recent) antibiotic use. *Data on the total numbers of residents invited during the study were missing, because not all participating NHs were able to provide complete data on numbers of newly admitted residents. For that reason, we show the average number of residents who lived in the participating wards during the study. †Residents who provided informed consent for participation in the situation that they would develop a possible UTI during the study period. ‡Primary analyses: suspected UTIs treated with AB. Secondary analyses: included UTIs regardless of treatment with AB.

antibiotics and included in the primary analysis. In the control group, this was 57 of the 106 cases (54%).

The mean age of included residents was 86 years, the majority were female (79%), and comorbidities were common (Table 1). We found that cases in the intervention group more often were women, more often had at least 1 risk factor for UTI, and more often had cardiovascular and pulmonary diseases. Cases in the control group more often had (very) severe dementia, more often resided on a psychogeriatric ward, and more often had an indwelling catheter.

Appropriate Antibiotic Prescribing

Of 114 suspected UTI cases treated with antibiotics in the intervention group, 62% of antibiotic prescriptions were appropriate. Of the 57 suspected UTI cases treated with antibiotics in the control group, this was 49% (difference: 13%). Table 2 shows that this difference was

not statistically significant (OR 1.43, 95% CI 0.57-3.62). Compared to the total group, we found larger between-group differences in appropriate antibiotic prescribing for residents with (very) severe dementia (ie, 17%; OR 3.36, 95% CI 0.86-13.13), and for residents with incontinence (ie, 17%; OR 4.28, 95% CI 0.96-18.99) (Table 2).

Changes in Treatment Decision, Complications, UTI Hospitalization, and Mortality

Intervention group physicians who did not start antibiotics at index consultation started antibiotics during follow-up in 16 of 75 cases (21%) and physicians of the control group in 11 of 49 cases (22%). Complications were rare in both groups: 2% of the residents in the intervention group and 3% of the residents in the control group had at least 1 complication, which were all reported for residents receiving antibiotic treatment (Table 3). Four residents in the intervention group

Table 1
Study Population* Demographic Characteristics

	Intervention Group		Control Group		Total		P Value (Treated With Antibiotics: Intervention vs Control)
	Overall (n = 189)	Treated With Antibiotics (n = 114)	Overall (n = 106)	Treated With Antibiotics (n = 57)	Overall (N = 295)	Treated With Antibiotics (n = 171)	
Mean age, y (SD)	87 (7)	87 (7)	84 (7)	85 (8)	86 (7)	86 (7)	.05
Female	160/189 (85)	96/114 (84)	73/105 (70)	39/57 (68)	233/294 (79)	135/171 (79)	.02
Residence on department for psychogeriatric illness	128/189 (68)	75/114 (66)	87/106 (82)	47/57 (83)	215/295 (73)	122/171 (71)	.02
(Very) severe dementia	69/182 (38)	36/109 (33)	56/96 (58)	39/54 (72)	125/278 (45)	75/163 (46)	<.001
Indwelling catheter	24/189 (13)	14/114 (12)	27/106 (26)	20/57 (35)	51/295 (17)	34/171 (20)	<.001
Risk factors for UTI [†]	107/189 (57)	68/114 (60)	49/106 (46)	28/57 (49)	156/295 (53)	96/171 (56)	.19
Cardiovascular disease	104/189 (55)	65/114 (57)	35/106 (33)	20/57 (35)	139/295 (47)	85/171 (50)	.01
Pulmonary disease	47/189 (25)	30/114 (26)	9/106 (9)	4/57 (7)	56/295 (19)	34/171 (20)	<.001
Consultation during evenings/weekend	32/189 (17)	21/114 (18)	6/106 (6)	4/57 (7)	38/295 (13)	25/171 (15)	.05

Unless otherwise noted, values are n/n (%).

*This concerns cases of suspected UTI for which antibiotics were prescribed; characteristics of unique patients instead of cases were similar.

[†]Risk factors for UTI: having recurrent UTI, renal or urinary tract abnormalities, diabetes mellitus, or compromised immunity (eg, due to radiation therapy or use of immunosuppressive medication).

had a possible UTI-related hospitalization (of which 3 received antibiotic treatment), vs 1 resident in the control group (not receiving antibiotic treatment). In both groups, 2% of the residents died of a possible UTI-related cause (all received antibiotic treatment).

Total Antibiotic Prescribing

In the 12 months prior to study onset, intervention group physicians prescribed more antibiotics compared with control group physicians (Figure 2). Prior to the study, there was a downward trend in total antibiotic prescribing in the intervention group and an upward trend in the control group. Right after study onset, there was a relatively large decrease in total antibiotic prescriptions in the intervention group, and a small decrease in the control group. After these decreases until study completion, the total of antibiotic prescriptions remained stable in both groups.

In the intervention group, there were 3.81 antibiotic prescriptions per 1000 residents care-days prior to study onset and 2.86 antibiotic prescriptions after study onset (0.95 decrease). In the control group, this was 2.55 prior to and 2.50 after study onset (0.05 decrease). In the intervention group, there were 1.53 UTI-related antibiotic prescriptions per 1000 resident care-days in the 12 months prior to study onset and 0.88 during the study (0.65 decrease). In the control group, this was 0.73 prior to and 0.75 during the study (0.02 increase). The differences in

pre-post study changes between the intervention and control group were significant for both the total antibiotic prescriptions and the UTI-related antibiotic prescriptions (P = .02 vs P = .02).

Discussion

This study evaluated the effect of an EHR-integrated decision tool for antibiotic treatment of suspected UTI in NH residents, accompanied by supportive interventions for physicians and nursing staff, on appropriate antibiotic prescribing for UTI. We found that antibiotics for UTI were more often appropriately prescribed in the intervention group; however, there was insufficient evidence of effect. Negative consequences for residents with suspected UTI, such as complications and UTI-related hospitalization and mortality, were rare and occurred almost all in patients who were prescribed antibiotics.

We consider 2 possible explanations for not finding sufficient evidence of effect. First, our study was underpowered as we were not able to include the number of cases defined in our sample size calculation. During the informed consent procedure, we learned that this low response was probably due to the patient information material often being misunderstood or considered “overwhelming.” Patient information material could, however, not be adjusted as we had to abide by Dutch legislation requiring very extensive information to be handed out.

Table 2
Appropriate Antibiotic Prescribing in Patients With Suspected UTI and Treated With Antibiotics, Intervention Group vs Control Group, Overall and Per Subgroup

	Intervention, n/n (%)	Control, n/n (%)	Descriptive					
			Model 1: Unadjusted			Model 2: Adjusted*		
			OR	95% CI	P Value	OR	95% CI	P Value
Overall	71/114 (62)	28/57 (49)	1.83	0.82–4.12	.14	1.43	0.57–3.62	.45
Per subgroup					P Value Interaction Term [†]			P Value Interaction Term [†]
(Very) severe dementia					.48			.46
Yes	22/36 (61)	17/39 (44)	2.38	0.77–7.39		3.36	0.86–13.13	
No	44/73 (60)	9/15 (60)	1.25	0.34–4.56		0.55	0.12–2.49	
Urine incontinence					.81			.56
Yes	25/42 (60)	9/21 (43)	2.24	0.66–7.62		4.28	0.96–18.99	
No	46/72 (64)	19/36 (53)	1.59	0.62–4.10		0.82	0.26–2.64	

*Adjusted for indwelling catheter, gender, (very) severe dementia, mean number of antibiotic prescriptions per 1000 resident-care days on the NH level in the 12 months prior to study onset, pulmonary diseases, consultation during evenings/weekend.

[†]Interaction term: Intervention × Group.

Table 3
Complications, Hospitalization, and Mortality in Patients With Suspected UTI, Intervention Group vs Control Group

	Intervention			Control		
	Total (n = 189)	Treated With Antibiotics (n = 114)	Not Treated With Antibiotics (n = 75)	Total (n = 106)	Treated With Antibiotics (n = 57)	Not Treated With Antibiotics (n = 49)
Any complications	3/179 (2)	3/108 (3)	0/71 (0)	3/101 (3)	3/53 (6)	0/48 (0)
Side effects antibiotics	0/179 (0)	0/108 (0)	0/71 (0)	1/101 (1)	1/53 (2)	0/48 (0)
Renal insufficiency	1/179 (1)	1/108 (1)	0/71 (0)	1/101 (1)	1/53 (2)	0/48 (0)
Pyelonephritis/urosepsis	3/179 (2)	3/108 (3)	0/71 (0)	2/101 (2)	2/53 (2)	0/48 (0)
UTI-related hospitalization	4/180 (2)	3/109 (3)	1/71 (1)	1/101 (1)	0/53 (0)	1/48 (2)
UTI-related mortality	4/182 (2)	4/109 (4)	0/73 (0)	2/101 (2)	2/53 (4)	0/48 (0)

Values are n/n (%).

Second, we initially aimed to conduct this study prior to publication of the updated national guideline, in which the decision tool subject to our study would be introduced,¹⁷ ensuring that only intervention group NHs had access to it. The guideline, however, became available before study onset, thus providing control group NHs access to the decision tool (albeit not EHR-integrated). Although we did not actively implement the guideline in these NHs, participating in the study may have increased awareness for appropriate antibiotic prescribing, especially since physicians of the control group also filled out CRFs. This may have motivated them to prescribe antibiotics more carefully and make efforts in familiarizing with this new guideline. If this will be confirmed in our forthcoming process evaluation study, this may have resulted in a smaller than anticipated difference in appropriate antibiotic prescribing between the groups.

Considering the above, our intervention could potentially still be beneficial. This may be further supported by the electronic prescribing system data, in which we observed a relatively large decrease in total antibiotic prescribing (for all and UTI-specific antibiotic types) in the intervention group. Future research, preferably under control group

circumstances with less intervention interference (such as – in our case – the recent introduction of a guideline including the decision tool central to the intervention) may elucidate whether comparable interventions may indeed improve appropriate antibiotic prescribing for suspected UTI among NH residents.

The percentage of 62% appropriate antibiotic prescribing in the intervention group is high compared to other studies reporting on proportions of appropriate antibiotic prescribing for UTI in the NH setting (range: 15%-56%).^{23–26} Comparison of these proportions is, however, complicated by the different criteria for appropriateness used and the difference in outcome measures. We chose to use ‘UTI treated with antibiotics’ as denominator of our outcome measure instead of ‘all suspected UTI’. Since our intervention actively steers on nonspecific S&S no longer being attributed to UTI, it is likely that the definition of ‘suspected UTI’ was more stringent in the intervention group than in the control group.

In both the intervention and the control group, there were few complications, UTI-related hospitalizations and mortality. Moreover, almost all negative consequences that were reported were in residents who did receive antibiotics at index consultation. It is therefore very

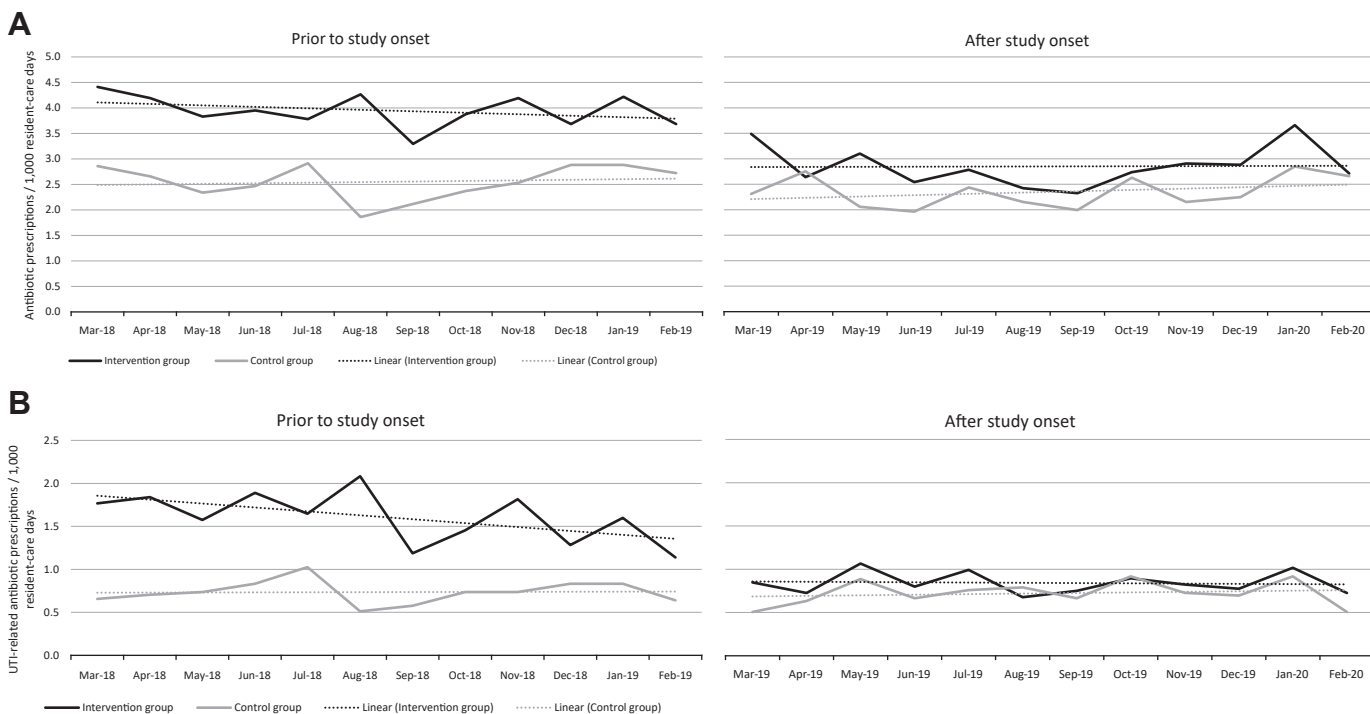


Fig. 2. (A) Total of antibiotic prescriptions per 1000 resident-care days per month in intervention and control group prior to study onset (March 2018–February 2019) and after study onset (March 2019–February 2020). (B) Total of UTI-related antibiotic prescriptions (ie, nitrofurantoin, fosfomycin, trimethoprim) per 1000 resident-care days per month in intervention and control group prior to study onset (March 2018–February 2019) and after study onset (March 2019–February 2020).

unlikely that withholding antibiotics in case of a suspected UTI poses residents at risk for adverse outcomes. This is in line with a previous study reporting on an antibiotic stewardship intervention that reduced antibiotic use in NH residents with “unlikely cystitis” without an increase in all-cause hospitalizations and mortality.²⁷

A strength of our study is that we developed a multidisciplinary intervention involving both physicians and nursing staff. Another strength was the efficient data collection through EHR-integrated CRFs, reducing chances of missing potential inclusions. Furthermore, as the EHR-integrated decision tool was combined with the process of data collection, all intervention group physicians that included residents in the study were automatically offered the treatment advice. This, however, does not guarantee that physicians actually used the tool in their treatment decision. It is possible that treatment decisions were made prior to entering the data in the EHR and thus before being confronted with the treatment advice. On the other hand, in these cases physicians may have used a nondigital version of the decision tool, for example, the pocket card handed out as a supportive intervention, in decision making. We aim to provide more clarity in these issues in our forthcoming process evaluation study.

Limitations of our study include the previously addressed small sample size; the use of “UTI treated with antibiotics” rather than “all suspected UTI” as a denominator in our study; and the potential influence of study participation on antibiotic prescribing in the control group. In addition, randomization turned out unfortunate as several patient characteristics differed between groups as well as total antibiotic-prescribing rates prior to study onset. Our analyses enabled adjustment for the most influential (including total antibiotic-prescribing rates), but not all baseline differences between intervention and control group. Finally, we did not validate the accuracy of data capture. We therefore cannot exclude the possibility of participant selection bias or misreporting.

Conclusion and Implications

Although there was an improvement in appropriate antibiotic prescribing in the intervention group, this does not provide sufficient evidence for our multidisciplinary intervention. Not finding evidence for a positive effect is probably a consequence of our relatively small sample size. Despite the inconclusive results, our intervention could potentially still be effective, because we established a large reduction in the number of antibiotic prescriptions in our intervention group.

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Supplementary Data

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References

1. Van Buul LW, van der Steen JT, Veenhuizen RB, et al. Antibiotic use and resistance in long term care facilities. *J Am Med Dir Assoc* 2012;13:568e1–568e13.
2. Van Buul LW, Veenhuizen RB, Achterberg WP, et al. Antibiotic prescribing in Dutch nursing homes: how appropriate is it? *J Am Med Dir Assoc* 2015;16:229–237.
3. D'Agata E, Loeb MB, Mitchell SL. Challenges in assessing nursing home residents with advanced dementia for suspected urinary tract infections. *J Am Geriatr Soc* 2013;61:62–66.
4. Juthani-Mehta M, Datunashvili A, Tinetti M. Tests for urinary tract infection in nursing home residents. *JAMA* 2014;312:1687e1688.
5. Fleming A, Bradley C, Cullinan S, Byrne S. Antibiotic prescribing in long-term care facilities: a meta-synthesis of qualitative research. *Drugs Aging* 2015;32:295–303.
6. Van Buul LW, van der Steen JT, Doncker SM, et al. Factors influencing antibiotic prescribing in long-term care facilities: a qualitative in-depth study. *BMC Geriatr* 2014;14:136.
7. Nace DA, Drinka PJ, Crnich CJ. Clinical uncertainties in the approach to long term care residents with possible urinary tract infection. *J Am Med Dir Assoc* 2014;15:133–139.
8. Ashraf MS, Gaur S, Bushen OY, et al. Diagnosis, treatment, and prevention of urinary tract infections in post-acute and long-term care settings: a consensus statement from AMDA's Infection Advisory Subcommittee. *J Am Med Dir Assoc* 2020;21:12–24.e2.
9. Biggel M, Heytens S, Latour K, Bruyndonckx R, Goossens H, Moons P. Asymptomatic bacteriuria in older adults: the most fragile women are prone to long-term colonization. *BMC Geriatr* 2019;19:170.
10. Hedin K, Petersson C, Wideback K, Kahlmeter G, Mölstedt S. Asymptomatic bacteriuria in a population of elderly in municipal institutional care. *Scand J Prim Health Care* 2002;20:166–168.
11. Juthani-Mehta M. Asymptomatic bacteriuria and urinary tract infection in older adults. *Clin Geriatr Med* 2007;23:585–594. vii.
12. Lin YT, Chen LK, Lin MH, Hwang SJ. Asymptomatic bacteriuria among the institutionalized elderly. *J Chin Med Assoc* 2006;69:213–217.
13. Hensgens MP, Goorhuis A, Dekkers OM, Kuijper EJ. Time interval of increased risk for *Clostridium difficile* infection after exposure to antibiotics. *J Antimicrob Chemother* 2012;67:742–748.
14. Donskey CJ. *Clostridium difficile* in older adults. *Infect Dis Clin North Am* 2017;31:743–756.
15. Van Buul LW, Vreeken HL, Bradley SF, et al. The development of a decision tool for the empiric treatment of suspected urinary tract infection in frail older adults: a Delphi consensus procedure. *J Am Med Dir Assoc* 2018;19:757–764.
16. Laka M, Milazzo A, Merlin T. Can evidence-based decision support tools transform antibiotic management? A systematic review and meta-analysis. *J Antimicrob Chemother* 2020;75:1099–1111.
17. Dutch Association of Elderly Care Physicians (Verenso). Guideline: urinary tract infections in frail older adults [Dutch]. <https://www.verenso.nl/richtlijnen-en-praktijkvoering/richtlijnenendatabase/urinegeweginfecties2018>. Accessed February 23, 2021.
18. Rutten JJS, van Buul LW, Smalbrugge M, et al. Antibiotic prescribing and non-prescribing in nursing home residents with signs and symptoms ascribed to urinary tract infection (ANNA): study protocol for a cluster randomized controlled trial. *BMC Geriatr* 2020;20:341.
19. Fleiss JL. *Statistical Methods for Rates and Proportions*. 1st ed. Wiley; 1981.
20. National Institute for Public Health and the Environment, Surveillance Network. Infectious diseases in nursing homes. Report 2012–2016 [Dutch]. https://www.rivm.nl/sites/default/files/201811/Referentiecijfers%20Incidentie%20SNIV%202011-2015_def.pdf. Accessed November 26, 2019.
21. Campbell MK, Fayers PM, Grimshaw JM. Determinants of the intracluster correlation coefficient in cluster randomized trials the case of implementation research. *Clin Trials* 2005;2:99–107.
22. Van der Weele TJ. Principles of confounder selection. *Eur J Epidemiol* 2019;34:211–219.
23. Loeb M, Simor AE, Landry L, et al. Antibiotic use in Ontario facilities that provide chronic care. *J Gen Intern Med* 2001;16:376–383.
24. Lim CJ, McLellan SC, Cheng AC, et al. Surveillance of infection burden in residential aged care facilities. *Med J Aust* 2012;196:327–331.
25. Pulia M, Kern M, Schwei RJ, Shah MN, Sampene E, Crnich CJ. Comparing appropriateness of antibiotics for nursing home residents by setting of prescription initiation: a cross-sectional analysis. *Antimicrob Resist Infect Control* 2018;7:74.
26. Eure T, LaPlace LL, Melchreit R, et al. Measuring antibiotic appropriateness for urinary tract infections in nursing home residents. *Infect Control Hosp Epidemiol* 2017;38:998–1001.
27. Nace DA, Hanlon JT, Crnich CJ, et al. A multifaceted antimicrobial stewardship program for the treatment of uncomplicated cystitis in nursing home residents. *JAMA Intern Med* 2020;180:944–951.