The Trial to Reduce Antimicrobial Use in Nursing Home Residents With Alzheimer Disease and Other Dementias (TRAIN-AD)  
A Cluster Randomized Clinical Trial

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**IMPORTANCE** Antimicrobials are extensively prescribed to nursing home residents with advanced dementia, often without evidence of infection or consideration of the goals of care.

**OBJECTIVE** To test the effectiveness of a multicomponent intervention to improve the management of suspected urinary tract infections (UTIs) and lower respiratory infections (LRIs) for nursing home residents with advanced dementia.

**DESIGN, SETTING, AND PARTICIPANTS** A cluster randomized clinical trial of 28 Boston-area nursing homes (14 per arm) and 426 residents with advanced dementia (intervention arm, 199 residents; control arm, 227 residents) was conducted from August 1, 2017, to April 30, 2020.

**INTERVENTIONS** The intervention content integrated best practices from infectious diseases and palliative care for management of suspected UTIs and LRIs in residents with advanced dementia. Components targeting nursing home practitioners (physicians, physician assistants, nurse practitioners, and nurses) included an in-person seminar, an online course, management algorithms (posters, pocket cards), communication tips (pocket cards), and feedback reports on prescribing of antimicrobials. The residents’ health care proxies received a booklet about infections in advanced dementia. Nursing homes in the control arm continued routine care.

**MAIN OUTCOMES AND MEASURES** The primary outcome was antimicrobial treatment courses for suspected UTIs or LRIs per person-year. Outcomes were measured for as many as 12 months. Secondary outcomes were antimicrobial courses for suspected UTIs and LRIs when minimal criteria for treatment were absent per person-year and burdensome procedures used to manage these episodes (bladder catheterization, chest radiography, venous blood sampling, or hospital transfer) per person-year.

**RESULTS** The intervention arm had 199 residents (mean [SD] age, 87.7 [8.0] years; 163 [81.9%] women; 36 [18.1%] men), of which 163 (81.9%) were White and 27 (13.6%) were Black. The control arm had 227 residents (mean [SD] age, 85.3 [8.6] years; 190 [83.7%] women; 37 [16.3%] men), of which 200 (88.1%) were White and 22 (9.7%) were Black. There was a 33% (nonsignificant) reduction in antimicrobial treatment courses for suspected UTIs or LRIs per person-year in the intervention vs control arm (adjusted marginal rate difference, −0.27 [95% CI, −0.71 to 0.17]). This reduction was primarily attributable to reduced antimicrobial use for LRIs. The following secondary outcomes did not differ significantly between arms: antimicrobials initiated when minimal criteria were absent, bladder catheterizations, venous blood sampling, and hospital transfers. Chest radiography use was significantly lower in the intervention arm (adjusted marginal rate difference, −0.56 [95% CI, −1.10 to −0.03]). In-person or online training was completed by 88% of the targeted nursing home practitioners.

**CONCLUSIONS AND RELEVANCE** This cluster randomized clinical trial found that despite high adherence to the training, a multicomponent intervention promoting goal-directed care for suspected UTIs and LRIs did not significantly reduce antimicrobial use among nursing home residents with advanced dementia.

**TRIAL REGISTRATION** ClinicalTrials.gov identifier: NCT03244917

Published online July 12, 2021.

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Infections and suspected infections are common in residents with advanced dementia. For those who reside in nursing homes, infection management is often characterized by antimicrobial misuse, emergence of multidrug-resistant organisms, use of burdensome procedures, and failure to consider goals of care. These residents also may not benefit clinically from treatment with antimicrobials, which are often prescribed without clinical evidence of a bacterial infection. Comfort is the most common goal of care for residents with advanced dementia, and the diagnostic evaluation and treatment of infections may not align with that goal.

Uptake of recently issued guidelines from the Centers for Disease Control and Prevention for antimicrobial stewardship in nursing homes has been inconsistent. Multicomponent nursing home interventions that have been tested in randomized clinical trials (RCTs) and have been shown to reduce antimicrobial use have not been adopted into practice. Despite the need to align antimicrobial use at the end-of-life with goals of care, efforts to improve infection management in nursing homes have not integrated infectious disease and palliative care principles nor have they focused on residents with advanced dementia.

The objective of the Trial to Reduce Antimicrobial Use in Nursing Home Residents With Alzheimer Disease and Other Dementias (TRAIN-AD) was to evaluate a multicomponent intervention to improve the management of suspected infections in nursing home residents with advanced dementia by merging best practices from infectious diseases and palliative care. This report presents the intervention’s effectiveness in reducing the primary outcome: antimicrobial treatment courses for suspected urinary tract infections (UTIs) or lower respiratory infections (LRIs). Secondary outcomes included (1) antimicrobial courses for suspected UTIs and LRIs when consensus-based minimal criteria to initiate treatment were absent, and (2) burdensome procedures used to evaluate these episodes.

Methods

The TRAIN-AD was conducted from August 7, 2017, and April 30, 2020. The study was reviewed and approved by Hebrew SeniorLife’s Institutional Review Board. Informed consent was waived because the TRAIN-AD was deemed to be of minimal risk per the Regulations for the Protection of Human Subjects (45 CFR §46). Printed flyers posted in facilities and mailed to proxies described how to opt-out of data collection. The study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline. The full trial design is detailed elsewhere and the trial protocol is available in Supplement 1.

Facilities and Randomization

Administrators of eligible nursing homes (>60 beds and within 60 miles of Boston) were mailed information and telephoned to solicit participation in the trial (Figure 1). Facility involvement included a 3-month start-up period and a 24-month implementation and data collection phase. Facilities were recruited in staggered waves every 4 months. In each wave, a statistician (M.L.S.) used a computer-generated algorithm to randomly allocate nursing homes to the intervention or control arm. Using data from Long-Term Care Focus, covariate-constrained randomization was used to minimize between-arm imbalances of characteristics potentially associated with advanced dementia care: a facility’s profit status and the number of Black residents per facility (dichotomized at the median). The number of residents with severe cognitive impairment per facility (dichotomized at the median) was also included in the covariate-constrained randomization to ensure a balance of these residents between arms.

Participants

Resident enrollment in the trial was open from October 1, 2017, to February 24, 2020. Eligibility criteria included being 60 years of age or older and having dementia (any type), a Global Deterioration Scale score of 7 (range, 1-7; higher scores indicate worse dementia), a length of stay greater than 90 days, and an English-speaking health care proxy. During study initiation at each facility and every 2 months for as many as 12 months, research assistants asked nurses to identify eligible residents and confirmed eligibility by chart review.

At intervention facilities, the infection preventionist or director of nursing was designated as the site champion. During implementation start-up at each facility and every 6 months thereafter, the site champion generated a list of nursing home practitioners to target: (1) nurses working at least 2 shifts weekly, caring for advanced dementia residents; and (2) prescribing medical practitioners (physicians, nurse practitioners, and physician assistants) caring for at least 2 residents with advanced dementia.

Intervention Structure and Implementation

During a 3-month facility start-up period, research and nursing home teams (eg, site champion, director of nursing, education specialists) cooperatively planned the intervention’s implementation. A protocol manual was provided. During implementation, the project director and site champion met monthly to problem-solve ongoing issues.
Intervention content integrated infectious diseases and palliative care best practices to improve management of suspected UTIs and LRIs in residents with advanced dementia. The infectious disease best practices centered on consensus-based minimal clinical criteria for empirical antimicrobial initiation in nursing homes that were adapted for residents with advanced dementia who cannot reliably communicate certain symptoms (eg, dysuria),\(^2,3,31\) Palliative care best practices focused on integrating residents’ preferences into treatment decisions and optimizing communication with their health care proxies.

Intervention components for targeting nursing home practitioners included: an in-person seminar, an online course, management algorithms (posters and pocket cards; Figure 2), proxy communication tips (eMethods in Supplement 2), and feedback reports for prescribing antimicrobials. A booklet about infections in residents with advanced dementia was mailed to each resident’s proxy. The components were developed by experts in geriatrics, infectious diseases, and palliative medicine, guided by the literature,\(^1,2,4,9,11,18,27,38-40\) and were refined based on peer review and pilot-testing. Practitioners made final management decisions.

At implementation start-up, targeted practitioners were asked to attend a 1-hour in-person training seminar describing the program and infection management principles delivered by 1 of 3 physician-educators who were board-certified in both geriatric and palliative medicine.\(^38\) Providers unable to attend the 1-hour seminar were offered a 10-minute 1-on-1 mini-orientation by either the site champion or project director. Seminars were repeated every 6 months at each nursing home to train new practitioners, answer questions, and reinforce the training of established practitioners. The site champion was an on-site resource for practitioners throughout the implementation period.

Practitioners were also asked to complete a 45-minute online course, *Infection Management in Advanced Dementia*,\(^41\) composed of 4 cases of nursing home residents with advanced dementia (2 with UTIs and 2 with LRIs). Three videos integrated into the cases demonstrated communication strategies for challenging conversations with proxies.\(^38\) Learners completed a 10-item pretest and posttest knowledge assessment (score range, 0%-100%) and could repeat the posttest until they obtained the required score of 75%. Learners had 3 months to complete the course. The research team emailed reminders to noncompliant practitioners and gave their names to the site champions. Providers completing the course received a $50 gift card and 1 Continuing Medical Education (medical practitioners) or 1 Continuing Education Unit (nurses). Chromebooks were raffled off among participating practitioners in facilities achieving 67% completion.

Treatment management algorithms for suspected UTIs and LRIs (Figure 2) were printed on posters that were hung in nursing home units and on laminated pocket cards given to targeted practitioners; these algorithms were also integrated with the online course. The algorithms operationalized 2 main considerations for antimicrobial use: (1) alignment with residents’ preferences, and (2) presence of consensus-based minimal criteria for treatment initiation.\(^2,3,30,31\) Individualized feedback reports were emailed to prescribing practitioners every 2 months describing suspected UTI or LRI episodes for which they had prescribed antimicrobials when minimal criteria for treatment were absent. Practitioners received pocket cards with tips for communicating with proxies about infection management (eMethods in the Supplement).\(^38\)

Residents’ proxies received a 6-page booklet by mail about infections in residents with advanced dementia, treatment...
options, and aligning treatment with goals of care. Practitioners were encouraged to review the booklets with proxies.

**Control Arm**
Facilities in the control arm continued routine care for suspected infections. No restrictions were placed in either arm with regard to other antimicrobial stewardship, advance care planning, or palliative care programs.

**Data Collection and Elements**
Data were abstracted from residents' charts at baseline, every 2 months and for as many as 12 months, and within 30 days of death. Baseline data included: age, sex, race/ethnicity (Asian, Black, Hispanic, White, and unknown/not reported), comorbidities (ie, congestive heart failure, chronic obstructive pulmonary disease, and diabetes mellitus), hospice enrollment, and advance directives not to hospitalize and/or to withhold anti-

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**Figure 2. Management Algorithms for Suspected Urinary Tract Infections (UTIs) and Lower Respiratory Infections (LRIs) in Nursing Home Residents With Advanced Dementia**

- **A** Suspected UTI
  - One of the following?
    - T ≥100.2°F or
    - 2°F > baseline
    - Rigors
  - Signs/symptoms of nonurinary tract infection?
  - Minimal criteria for the initiation of antimicrobials are met?
  - Patient preferences include use of antimicrobials?
  - Results:
    - UA negative, culture negative
    - UA positive, c culture negative
    - UA negative, culture positive
  - Do not send urine specimen or start antimicrobials
  - Send urine for UA and culture
  - Do not send urine specimen. Evaluate for other infection.

- **B** Suspected LRI
  - T ≥102°F
  - One of the following?
    - RR > 25 breaths/min
    - New/increased productive cough
  - New or increased productive cough?
  - Evaluate for other infection
  - Minimal criteria for the initiation of antimicrobials are met?
  - Patient preferences include use of antimicrobials?
  - Do not start antimicrobials
  - Start antimicrobials

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CFU denotes colony-forming units; HR, heart rate; RR, respiratory rate; T, temperature; and UA, urine analysis.

a Algorithm applies to residents with dementia who are unable to meaningfully communicate information about symptoms typical of a UTI (eg, dysuria, suprapubic pain). The presence or absence of cloudy and/or odorous urine alone should not be used as an indication to send a urine specimen for evaluation or to start an antimicrobial.

b Without an indwelling urinary catheter, mental status change alone is not an adequate symptom to support a diagnosis of a UTI.

c Antimicrobials may be initiated empirically while urine specimen results are pending.

d Positive urinalysis / 10,000 white blood cells/L or dipstick results positive for white blood cells, leukocyte esterase, or nitrites.

e Positive urine culture: no indwelling urinary catheter 10³ CFU/mL of 1 bacterial organism; with indwelling urinary catheter 10³ CFU/mL.

f A complete blood cell count with differential and chest radiography may not be required for empiric antimicrobial treatment.
microbials (ie, intravenous, intramuscular, or any route). Nurses rated each resident’s functional status by using the Bedford Alzheimer Nursing Severity Subscale (range, 7-28 points; higher scores indicate more disability). When applicable, date of death was ascertained from the resident’s chart.

At all follow-up assessments, 2 research assistants independently identified suspected UTIs and LRIs that occurred during the intervening period based on progress notes, tests (eg, urine cultures), and antimicrobial use. Inconsistencies were resolved by the nurse project director. Data abstracted for each episode included: signs (eg, temperature, respiratory rate), symptoms (eg, cough), and burdensome procedure use (ie, bladder catheterization, venous blood sampling, chest radiography, and hospital transfer). Suspected diagnosis and administration dates were collected for all antimicrobial courses. A 3-day treatment-free interval defined a separate antimicrobial course. More than 1 antimicrobial on a given day was considered a single course. Based on documented signs and symptoms, suspected UTIs and LRIs that were treated were categorized as meeting or not meeting consensus-based minimal criteria to initiate antimicrobials.

Outcomes

The outcomes were measured for as many as 12 months. The primary outcome was the number of antimicrobial courses for suspected UTIs or LRIs per person-year. The secondary outcomes were (1) the number of antimicrobial courses for suspected UTIs or LRIs per person-year when minimal criteria for initiation were absent and (2) the number of burdensome procedures (ie, bladder catheterization, venous blood draw, chest radiography, or hospital transfer) used to evaluate suspected UTIs or LRIs per person-years. Exploratory analyses examined antimicrobial courses prescribed for any indication per person-year.

Statistical Analysis

Analyses were performed November 1, 2017, to January 22, 2021, using SAS, version 9.4 (SAS Institute Inc), Stata, release 13.1 (StataCorp LLC), and R, version 3.4.1 (The R Foundation for Statistical Computing). Frequencies described categorical variables and means with SDs or SEs described continuous variables. Analyses were conducted at the resident-level, followed intention-to-treat principles, and adjusted for clustering within nursing homes using robust estimates of variance. Adjusted analyses included covariates considered in the constrained randomization: facility profit status and resident’s race/ethnicity (Black or any other).

Negative binomial-logit hurdle regression models tested the intervention’s effect on all outcomes. This 2-part model included a logit model examining the probability of receiving at least 1 antimicrobial course, and a truncated negative binomial model examining the number of courses. Follow-up time was included as an offset. A 2-tailed test of the difference in adjusted marginal means examined the null hypothesis using a level of significance of $P < .05$. Bootstrapped SEs were obtained by resampling clusters, estimating the specified model for each bootstrap sample, and combining all estimates for the bootstrap samples. Adjusted marginal rate differences with 95% CIs were generated using the bootstrapped SEs.

Sample Size

Calculations were based on count regression adding a design effect to account for facility-level clustering. Assumed 2-sided testing, type I error rate of 5%, and 90% power. Based on prior research, we assumed an intracluster correlation of 0.01, 15 residents per facility, an average of 0.79 person-years per resident, and 1.26 antimicrobial courses for suspected UTIs or LRIs per person-year in the control arm. We estimated that a sample size of 410 residents from 28 facilities (205 residents from 14 facilities per arm) was needed to achieve an absolute reduction of 0.38 (total reduction of 30%) for the primary outcome in the intervention vs control arm.

Masking

Research implementation team members could not be masked. The 2 research assistants who enrolled residents and collected their data, the principal investigator (S.L.M.), the statistician (M.L.S.), and the data programmers (D.A.H. and T.T.) were masked.

Results

Recruitment and Follow-up

At the 113 eligible nursing homes, 81 administrators could not be contacted or they declined participation (Figure 1), leaving 32 randomized facilities (intervention, n = 17; control, n = 15). At that time, 22 residents were still being followed and had completed these assessments: 10 months, n = 3; 8 months, n = 16; and 2 months, n = 3. There were 201 eligible residents in the intervention arm and 227 in the control arm (Figure 1). Two residents in the intervention arm and 1 in the control arm had a baseline assessment but no follow-up assessment and were excluded. One proxy opted out in the control arm. The final analytic sample included 199 residents in the intervention arm and 227 residents in the control arm. Because of the COVID-19 lockdown of Boston nursing homes, data collection ceased on March 10, 2020, slightly earlier than planned. At that time, 22 residents were still being followed and had completed these assessments: 10 months, n = 3; 8 months, n = 16; and 2 months, n = 3.

Resident Characteristics

As shown in Table 1, baseline demographic characteristics of residents in the intervention and control arms, respectively, were: mean age (SD), 87.7 (8.0) and 85.3 (8.6) years; 36 (18.1%) and 37 (16.3%) were men; 163 (81.9%) and 190 (83.7%) were women; 27 (13.6%) and 22 (9.7%) were Black; and 163 (81.9%) and 37 (16.3%) were men; 163 (81.9%) and 190 (83.7%) were women; 27 (13.6%) and 22 (9.7%) were Black; and 163 (81.9%) and 37 (16.3%) were women; 27 (13.6%) and 22 (9.7%) were Black; and 163 (81.9%) and 37 (16.3%) were women; 27 (13.6%) and 22 (9.7%) were Black; and 163 (81.9%) and 37 (16.3%) were women; 27 (13.6%) and 22 (9.7%) were Black; and 163 (81.9%) and 37 (16.3%) were women; 27 (13.6%) and 22 (9.7%) were Black; and 163 (81.9%) and 37 (16.3%) were women; 27 (13.6%) and 22 (9.7%) were Black; and 163 (81.9%) and 37 (16.3%) were women; 27 (13.6%) and 22 (9.7%) were Black; and 163 (81.9%) and 37 (16.3%) were women; 27 (13.6%) and 22 (9.7%) were Black; and 163 (81.9%) and 37 (16.3%) were women; 27 (13.6%) and 22 (9.7%) were Black; and 163 (81.9%) and 37 (16.3%) were women; 27 (13.6%) and 22 (9.7%) were Black; and 163 (81.9%) and 37 (16.3%) were women; 27 (13.6%) and 22 (9.7%) were Black; and 163 (81.9%) and 37 (16.3%) were women; 27 (13.6%) and 22 (9.7%) were Black; and 163 (81.9%) and 37 (16.3%) were women; 27 (13.6%) and 22 (9.7%) were Black; and 163 (81.9%) and 37 (16.3%) were women; 27 (13.6%) and 22 (9.7%) were Black; and 163 (81.9%)
and 200 (88.1%) were White. Do-not-hospitalize orders were common but directives to withhold antimicrobial use were rare. Residents in both arms died: 82 (41.2%) in the intervention and 102 (44.9%) in the control arm.

Practitioner Characteristics and Participation
There were 387 nursing home practitioners targeted in the intervention facilities (median [range], 27.5 [11-47] practitioners per facility) among whom 303 were nurses (78.3%) and 84 (21.7%) were prescribing practitioners (physicians, 38 [9.8%]; nurses, 44 [11.4%]; physician assistants, 2 [0.5%]). A total of 329 practitioners (85%) were on-boarded when implementation began in their nursing home, and 58 (15%), after implementation had started.

A total of 342 (88.4%) of practitioners completed either the online course or the training seminar, with 247 (63.8%) completing both activities. Among the 303 nurses, 288 (95%) completed either the online course or the training seminar, and 197 (65%) completed both activities. Among the 84 prescribing practitioners, 68 (81%) completed either the online course or the training seminar, and 52 (62%) completed both activities. For the online course, the mean (SD) pretest and posttest scores were 59% (21%) and 95% (7%), respectively.

Outcomes
During the 12-month study period, 27.1% and 33.9% of residents in the intervention and control facilities, respectively, received at least 1 antimicrobial treatment course for a suspected UTI or LRI (Table 2). For the primary outcome, antimicrobial courses for suspected UTIs or LRIs per person-year was 33% lower in the intervention arm and 1.23 (0.34) in the control arm. The adjusted marginal rate of antimicrobial courses for suspected UTIs and LRIs per person-year was 33% lower in the intervention (0.55; 95% CI, 0.25 to 0.84) vs the control arm (0.82; 95% CI, 0.49 to 1.14), but the difference was not significant (adjusted marginal rate difference, −0.27; 95% CI, −0.71 to 0.17; P = .23); the intraclass correlation for the primary outcome was 0.03. There was a nonsignificant reduction in the adjusted marginal rates of antimicrobial courses for suspected UTIs or LRIs when minimal criteria for treatment were absent per person-year in the intervention vs control arm (Table 2).

The reduction in antimicrobial courses in the intervention vs control arm was more marked for suspected LRIs (Table 2). Exploratory analysis revealed a nonsignificant reduction of 31% in the adjusted marginal rates of antimicrobial courses for any indication per person-year in the intervention vs control arm (adjusted marginal rate difference, −0.37; 95% CI, −0.71 to 0.17; P = .23) and its reduction in the intervention arm (estimated, 30%; actual, 33%). However, a larger than anticipated intraclass correlation (estimated, 0.01; actual, 0.03) and varied number of

### Table 1. Baseline Characteristics of Nursing Home Residents and 12-Month Follow-up

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Intervention (n = 199)</th>
<th>Control (n = 227)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>87.7 (8.0)</td>
<td>85.3 (8.6)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>163 (81.9)</td>
<td>190 (83.7)</td>
</tr>
<tr>
<td>Men</td>
<td>36 (18.1)</td>
<td>37 (16.3)</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>163 (81.9)</td>
<td>200 (88.1)</td>
</tr>
<tr>
<td>Black</td>
<td>27 (13.6)</td>
<td>22 (9.7)</td>
</tr>
<tr>
<td>Asian</td>
<td>4 (2.0)</td>
<td>2 (0.9)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>3 (1.5)</td>
<td>0</td>
</tr>
<tr>
<td>Unknown/not reported</td>
<td>2 (1.0)</td>
<td>3 (1.3)</td>
</tr>
<tr>
<td>Alzheimer dementia (vs other dementia)</td>
<td>89 (44.7)</td>
<td>130 (57.3)</td>
</tr>
<tr>
<td>Comorbid conditions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>26 (13.1)</td>
<td>30 (13.2)</td>
</tr>
<tr>
<td>COPD</td>
<td>17 (8.5)</td>
<td>9 (4.0)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>47 (23.6)</td>
<td>44 (19.4)</td>
</tr>
<tr>
<td>Hospice enrolment</td>
<td>34 (17.1)</td>
<td>34 (15.0)</td>
</tr>
<tr>
<td>Advance directives</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No hospitalization</td>
<td>103 (51.8)</td>
<td>142 (62.6)</td>
</tr>
<tr>
<td>No intravenous antimicrobials</td>
<td>3 (1.5)</td>
<td>7 (3.1)</td>
</tr>
<tr>
<td>No intramuscular antimicrobials</td>
<td>2 (1.0)</td>
<td>4 (1.8)</td>
</tr>
<tr>
<td>No antimicrobials (any route)</td>
<td>1 (0.5)</td>
<td>2 (0.9)</td>
</tr>
<tr>
<td>Alzheimer severity subscale, a mean (SD)</td>
<td>19.6 (2.3)</td>
<td>20.4 (2.3)</td>
</tr>
<tr>
<td>Died during follow-up</td>
<td>82 (41.2)</td>
<td>102 (44.9)</td>
</tr>
<tr>
<td>Days of follow-up, median (IQR)</td>
<td>360 (144-367)</td>
<td>351 (116-362)</td>
</tr>
</tbody>
</table>

Abbreviations: COPD, chronic obstructive pulmonary disease; IQR, interquartile range.

* Bedford Alzheimer Nursing Severity Subscale, range 7-28; higher scores indicate more functional disability.32

### Discussion
This cluster RCT found a 33% (statistically nonsignificant) reduction in antimicrobial courses for suspected UTIs and LRIs among residents with advanced dementia in nursing homes randomized to the TRAIN-AD intervention vs routine care. This reduction was primarily attributable to fewer antimicrobial courses for suspect LRIs, in keeping with a significant reduction in chest radiography use in the intervention arm. There was high practitioner adherence to the training components of the TRAIN-AD intervention.

Interpretation of these findings merits several considerations. While most outcomes trended in a direction reflecting less intensive care for suspected infections in the intervention arm, insufficient power may have accounted for the fact that these reductions, except for chest radiography use, were not statistically significant. Key assumptions in the power calculations were accurate, including the unadjusted rate of the primary outcome in the control arm (estimated, 1.26; actual, 1.23) and its reduction in the intervention arm (estimated, 30%; actual, 33%). However, a larger than anticipated intraclass correlation (estimated, 0.01; actual, 0.03) and varied number of
Table 2. Antimicrobial Treatment Courses Among Nursing Home Residents With Advanced Dementia During the 12-Month Study Period

<table>
<thead>
<tr>
<th>Indication</th>
<th>Residents receiving ≥1 course, No. (%)</th>
<th>Adjusted marginal rate of antimicrobial courses per person-year (SE) [95% CI]</th>
<th>Adjusted marginal rate difference (SE) [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention (n = 199)</td>
<td>Control (n = 227)</td>
<td>Intervention (n = 199)</td>
</tr>
<tr>
<td>For suspected UTIs or LRIs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antimicrobial courses</td>
<td>54 (27.1)</td>
<td>77 (33.9)</td>
<td>0.55 (0.15) [0.25 to 0.84]</td>
</tr>
<tr>
<td>Antimicrobial courses when minimal criteria for treatment absent</td>
<td>41 (20.6)</td>
<td>50 (22.0)</td>
<td>0.37 (0.11) [0.15 to 0.60]</td>
</tr>
<tr>
<td>For suspected LRIs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antimicrobial courses</td>
<td>36 (18.1)</td>
<td>60 (26.4)</td>
<td>0.32 (0.09) [0.13 to 0.50]</td>
</tr>
<tr>
<td>Antimicrobial courses when minimal criteria for treatment absent</td>
<td>25 (12.6)</td>
<td>33 (14.5)</td>
<td>0.15 (0.05) [0.05 to 0.25]</td>
</tr>
<tr>
<td>For suspected UTIs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antimicrobial courses</td>
<td>25 (12.6)</td>
<td>26 (11.5)</td>
<td>0.20 (0.06) [0.08 to 0.32]</td>
</tr>
<tr>
<td>Antimicrobial courses when minimal criteria for treatment absent</td>
<td>17 (8.4)</td>
<td>19 (8.4)</td>
<td>0.09 (0.03) [0.03 to 0.16]</td>
</tr>
<tr>
<td>For any indication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antimicrobial courses</td>
<td>70 (35.2)</td>
<td>95 (41.9)</td>
<td>0.82 (0.15) [0.52 to 1.13]</td>
</tr>
</tbody>
</table>

Abbreviations: LRI, lower respiratory infection; UTI, urinary tract infection.  
A Adjusted for facility profit status, resident race (Black vs other).  
b Marginal rate difference is expressed as intervention minus control.  
c Primary trial outcome, P = .23.  
d Minimal criteria for treatment based on consensus guidelines.2,30,31

Table 3. Burdensome Procedures Used to Manage Suspected Urinary Tract or Lower Respiratory Infections Among Nursing Home Residents With Advanced Dementia During the 12-Month Study Period

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Residents experiencing ≥1 procedure, No. (%)</th>
<th>Adjusted marginal rate of procedures per person-year (SE) [95% CI]</th>
<th>Adjusted marginal rate difference (SE) [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention (n = 199)</td>
<td>Control (n = 227)</td>
<td>Intervention (n = 199)</td>
</tr>
<tr>
<td>Any procedurea</td>
<td>81 (40.7)</td>
<td>112 (49.3)</td>
<td>1.07 (0.27) [0.54 to 1.60]</td>
</tr>
<tr>
<td>Bladder catheterizationb</td>
<td>49 (24.6)</td>
<td>45 (19.8)</td>
<td>0.47 (0.13) [0.21 to 0.73]</td>
</tr>
<tr>
<td>Chest radiography</td>
<td>53 (26.6)</td>
<td>91 (40.1)</td>
<td>0.53 (0.15) [0.24 to 0.83]</td>
</tr>
<tr>
<td>Venous blood sampling</td>
<td>60 (30.2)</td>
<td>74 (32.6)</td>
<td>0.64 (0.19) [0.28 to 1.00]</td>
</tr>
<tr>
<td>Hospital transfer</td>
<td>23 (11.6)</td>
<td>20 (8.8)</td>
<td>0.18 (0.07) [0.04 to 0.31]</td>
</tr>
</tbody>
</table>

Abbreviations: LRI, lower respiratory infection; UTI, urinary tract infection.  
A Adjusted for facility profit status, resident race (Black vs other).  
b Any procedure includes bladder catheterization, venous blood sampling, chest radiography, and hospital transfer.  
c Bladder catheterization to obtain a urine specimen for urinalysis and/or urine culture.
time, and the degree to which they enacted training principles when managing infections. Thus, it is possible that suboptimal intervention fidelity contributed to the nonsignificant findings. Ongoing analyses will examine whether specific training components, the “dose” of training (ie, completion of 1 or both training opportunities, mini vs full seminar), or practitioner type influenced the effectiveness of the intervention.

Limitations
Several limitations deserve comments. Findings may not be generalizable outside of Boston. Inadequate power and suboptimal implementation fidelity may have accounted for the nonsignificant findings. In addition, the intervention may have led to differential documentation of suspected infections between arms. However, antimicrobial use was reduced for all indications in the intervention vs the control arm (eg, not just UTIs or LRIs), thus this possibility was likely not an important source of bias.

Conclusions
The TRAIN-AD study demonstrated that training to promote a patient-centered and clinically sound approach to infection management in residents with advanced dementia can be delivered to nursing home practitioners. However, the effectiveness of the TRAIN-AD intervention to reduce antimicrobial use remains inconclusive. The TRAIN-AD highlighted critical design considerations for cluster RCTs of complex interventions, particularly conservative estimation of the intraclass correlation, and a priori inclusion of implementation fidelity evaluation grounded in comprehensive frameworks. Nonetheless, signals of effectiveness, high adherence to training, and the clinical importance of infection management in residents with advanced dementia merit consideration of a larger RCT testing an adapted TRAIN-AD intervention implemented in a nursing home health care system.

References


