

Antimicrobial Use for Symptom Management in Patients Receiving Hospice and Palliative Care: A Systematic Review

The Faculty of Oregon State University has made this article openly available.
Please share how this access benefits you. Your story matters.

Citation	Rosenberg, Joseph H., Albrecht, Jennifer S., Fromme, Erik K., Noble, Brie N., McGregor, Jessina C., Comer, Angela C., and Furuno, Jon P. <i>Journal of Palliative Medicine</i> . December 2013, 16(12): 1568-1574. doi:10.1089/jpm.2013.0276
DOI	10.1089/jpm.2013.0276
Publisher	Mary Ann Liebert, Inc.
Version	Version of Record
Citable Link	http://hdl.handle.net/1957/47061
Terms of Use	http://cdss.library.oregonstate.edu/sa-termsfuse

Antimicrobial Use for Symptom Management in Patients Receiving Hospice and Palliative Care: A Systematic Review

Joseph H. Rosenberg, BS,¹ Jennifer S. Albrecht, PhD,¹ Erik K. Fromme, MD, MCR,^{2,3} Brie N. Noble, BS,⁴
Jessina C. McGregor, PhD,⁴ Angela C. Comer, MPH,¹ and Jon P. Furuno, PhD⁴

Abstract

Background: Patients receiving hospice or palliative care often receive antimicrobial therapy; however the effectiveness of antimicrobial therapy for symptom management in these patients is unknown.

Objective: The study's objective was to systematically review and summarize existing data on the prevalence and effectiveness of antimicrobial therapy to improve symptom burden among hospice or palliative care patients.

Design: Systematic review of articles on microbial use in hospice and palliative care patients published from January 1, 2001 through June 30, 2011.

Measurements: We extracted data on patients' underlying chronic condition and health care setting, study design, prevalence of antimicrobial use, whether symptom response following antimicrobial use was measured, and the method for measuring symptom response.

Results: Eleven studies met our inclusion criteria in which prevalence of antimicrobial use ranged from 4% to 84%. Eight studies measured symptom response following antimicrobial therapy. Methods of symptom assessment were highly variable and ranged from clinical assessment from patients' charts to the Edmonton Symptom Assessment Scale. Symptom improvement varied by indication, and patients with urinary tract infections (two studies) appeared to experience the greatest improvement following antimicrobial therapy (range 67% to 92%).

Conclusion: Limited data are available on the use of antimicrobial therapy for symptom management among patients receiving palliative or hospice care. Future studies should systematically measure symptom response and control for important confounders to provide useful data to guide antimicrobial use in this population.

Introduction

HOSPICE AND PALLIATIVE CARE UTILIZATION is expected to increase with the aging of the U.S. population and increases in the prevalence of chronic and/or terminal diseases including cancer, chronic obstructive pulmonary disease, and dementia.^{1,2} Hospice and palliative care patients are at high risk for infection, and we recently published data to suggest that 27% of hospice patients received antibiotics in the final week of life.³ Despite this high prevalence, indications for antimicrobial therapy in hospice care remain unclear in a setting where death is expected and the benefits of antimicrobial therapy are not well understood. Potential negative consequences of antimicrobial use in this population include

medication side effects and adverse events, necessitating use of invasive devices, increased risk of subsequent opportunistic infections, and prolongation of an undesirable dying process.⁴ In addition, the use of potentially unnecessary antimicrobial therapy increases selective pressure and subsequent development of antimicrobial-resistant organisms.

In 2002, Nagy-Agren and Haley published a systematic review assessing infection management in palliative care patients with advanced cancer.⁵ In that study they reported that between 60% and 72% of patients with suspected infections were treated with antibiotics; however, only one study was reported to have examined whether antibiotic use improved patients' symptoms. In the past ten years several new studies examining infection management in palliative care patients

¹Department of Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore, Maryland.

²Division of Hematology and Medical Oncology, Knight Cancer Institute, ³Center for Ethics in Health Care, Oregon Health and Science University, Portland, Oregon.

⁴Department of Pharmacy Practice, Oregon State University/Oregon Health and Science University College of Pharmacy, Portland, Oregon.

Accepted July 22, 2013.

have been published. Therefore, we systematically reviewed the literature on antimicrobial use among adult patients with any diagnosis who were receiving palliative or hospice care with the objective of summarizing existing data on the use of antimicrobial therapy to improve symptom burden and the methods used to measure symptom improvement. These data are needed to guide antimicrobial therapy in this patient population.

Methods

Study identification

We queried the National Library of Medicine using the PubMed database for English-language articles published from January 1, 2001 through June 30, 2011. Limits were set to restrict the search to original research articles published in English and involving human subjects. The following search terms were used: (palliative care OR terminal care OR hospice care OR end-of-life) AND (infection OR antibiotic OR antifungal OR anti-infective). Additional studies were identified by a review of references from all retrieved articles.

Articles were included in this review if they provided data on antimicrobial use in patient populations under hospice or palliative care. We excluded studies that assessed only the use of antimicrobial wound dressings or mouthwashes as well as studies focusing strictly on pharmacokinetics of antimicrobials or environmental decontamination. Survey-based studies evaluating clinician decision making regarding antimicrobial prescription, without data on actual antimicrobials prescribing, and review articles were also excluded.

One author (J.H.R.) independently reviewed all articles and abstracts retrieved through the initial search to identify those meeting inclusion and exclusion criteria. Identified publications were further reviewed by two other authors (J.S.A. and B.N.N.). A fourth author (J.P.F.) resolved any discrepancies between reviewers. This study was determined to be exempt from institutional review board approval.

Data extraction and analysis

The following information was extracted from articles meeting the inclusion criteria: author(s), location of study, year of publication, sample size, patient population (underlying chronic condition and health care setting), study design, whether infective symptom response following antimicrobial use was reported, method for assessing symptom response, whether prophylactic antimicrobial use was reported or included in analysis, and the prevalence of antimicrobial use. Prevalence of antimicrobial use was based either on patients or infective episodes. Prevalence of antimicrobial use was calculated based on the text of the article in cases where it was not explicitly reported in order to provide a homogenous depiction of the outcome.

For studies reporting symptom response, the following additional information was extracted: definition of symptom response, indication for antimicrobial use (infection site), and results regarding symptom response. For three studies, we recalculated the proportion of patients in whom symptom improvement was observed to generate measures of effect comparable to that of the other studies.⁶⁻⁸ We calculated 95% confidence intervals for sample proportions using the exact binomial method to provide precision of estimation.

Results

We identified 984 articles in the National Library of Medicine database that met the search criteria. After reviewing these articles and those that were cross-referenced, we identified 11 publications that met all study criteria and which were therefore included in our systematic review.⁶⁻¹⁶ Characteristics of these studies are displayed in Table 1. Sample size ranged from 70 to 1598 patients (median=150 patients). Six of the studies were conducted in North America,^{10,11,13-16} one in Europe,⁶ three in Asia,^{8,9,12} and one in Australia.⁷ Six studies were conducted in hospitals,^{7-10,12,13} two in home-based hospice programs,^{15,16} one in an inpatient hospice,⁶ one in a long-term care facility,¹¹ and one study was conducted in multiple care settings (acute hospital, tertiary palliative care unit, and hospice).¹⁴

Four studies were prospective^{7,13,15,16} and seven studies were retrospective.^{6,8-12,14} Six studies included only cancer patients.^{8,12-16} Four studies included all primary diagnoses requiring palliative care or consult.^{6,7,9,10} One study included only dementia patients.¹¹ Only one study reported prophylaxis as an indication for antimicrobial prescription, citing use in two patients for traumatic urinary catheter insertion.⁷ The remaining 10 studies reported only therapeutic antimicrobial use.^{6,8-16}

Prevalence of antimicrobial use

Among the six studies that only included patients with cancer,^{8,12-16} the prevalence of antimicrobial use in patients receiving palliative care ranged from 19%¹³ to 84%.⁸ Among patients with documented infective episodes, 92%¹⁵ to 100%¹³ were treated with antimicrobial therapy.

In the five studies that included all diagnoses, the prevalence of antimicrobial use varied by route of administration and indication for use.^{6,7,9-11} Brabin and colleagues⁶ and Clayton and colleagues⁷ focused exclusively on patients who received parenteral antimicrobial therapy and reported prevalence of 9% and 4%, respectively. Chen and colleagues⁹ focused specifically on fever episodes as the indication for antimicrobial therapy and observed that 85% were treated with antimicrobials. The remaining two studies by Chun and colleagues¹⁰ and Evers and colleagues¹¹ reported antimicrobial use regardless of indication for use or route of administration and both observed that 53% of palliative care patients received antimicrobials.

When comparing antimicrobial use by setting of care, hospital-based studies^{7-10,12,13} reported the prevalence of antimicrobial use ranged from 4%¹³ to 97.5%¹² compared to studies set in hospices,^{6,15,16} where the reported prevalence ranged from 8.6%⁶ to 37%.¹⁵

Studies reporting symptom response

Eight studies reported some measure of symptom response.^{6-9,12,13,15,16} Of these, five included only cancer patients,^{8,12,13,15,16} and three included all primary diagnoses requiring palliative care.^{6,7,9} Four of the studies were prospective^{7,13,15,16} and four were retrospective.^{6,8,9,12}

Studies varied in their definitions of symptom response, as well as the extent to which they reported the specific symptoms assessed. Two studies clearly listed all symptoms assessed for response^{15,16} and one study included a partial list.⁸ In the retrospective studies, medical charts were reviewed for documentation of improvement in infective symptoms.^{6,8,9,12}

TABLE 1. STUDY CHARACTERISTICS AND PREVALENCE OF ANTIMICROBIAL USE FOR THE 11 ARTICLES MEETING THE INCLUSION CRITERIA

	<i>Patients</i>	<i>Primary diagnosis</i>	<i>Setting</i>	<i>Country</i>	<i>Study design</i>	<i>Symptom response reported</i>	<i>Prevalence of antimicrobial use</i>
Brabin and Allsopp et al. (2008)	209 pts	Mixed	Inpatient hospice and palliative care unit	United Kingdom	Retrospective	Yes	<ul style="list-style-type: none"> • 8.6% of 209 pts admitted during a six-month period¹
Chen et al. (2002)	88 pts 93 episodes of fever	Mixed	Hospice and palliative care unit in an acute care hospital	Taiwan	Retrospective	Yes	<ul style="list-style-type: none"> • 85% of 93 fever episodes during a hospital admission during a two-year period
Chun et al. (2010)	131 pts 92 infective episodes	Mixed	Palliative care unit in hospital	United States	Retrospective	No	<ul style="list-style-type: none"> • 53% of 131 inpatients who received palliative care consults during a six-month period
Clayton et al. (2003)	913 pts	Mixed	Hospice and palliative care unit in hospital	Australia	Prospective	Yes	<ul style="list-style-type: none"> • 4% of 913 admissions during a 13-month period
Evers et al. (2002)	303 pts	Dementia	Long-term care facility	United States	Retrospective	No	<ul style="list-style-type: none"> • 53% of 279 pts during the last six months of life
Lam et al. (2005)	70 pts 120 infective episodes	Cancer	Palliative care unit in an acute care hospital	Hong Kong	Retrospective	Yes	<ul style="list-style-type: none"> • 97.5% of 120 infective episodes during a seven-month period
Mirhosseini et al. (2006)	139 pts 31 infective episodes	Cancer	Palliative care unit in hospital	Canada	Prospective	Yes	<ul style="list-style-type: none"> • 19% of 139 pts admitted in a 10-month period • 100% of 31 infective episodes
Oh et al. (2006)	141 pts	Cancer	Acute care hospital receiving supportive care only	South Korea	Retrospective	Yes	<ul style="list-style-type: none"> • 84.4% of 141 pts who died during a hospital stay during 14-month period
Oneschuk et al. (2002)	50 pts in each setting 150 total	Cancer	Palliative care unit/acute care hospital/hospice	Canada	Retrospective	No	<ul style="list-style-type: none"> • 58% of 50 consecutive pts in the acute care hospital • 52% of 50 consecutive pts in a tertiary palliative care unit • 22% of 50 consecutive pts in hospice
Reimbolt et al. (2005)	1598 pts 685 infective episodes	Cancer	Outpatient hospice and palliative care unit	United States	Prospective	Yes	<ul style="list-style-type: none"> • 37% of 1598 pts during a 24-month period • 92% of 685 infective episodes during a 24-month period
White et al. (2003)	255 pts 129 infective episodes	Cancer	Outpatient hospice and palliative care unit	United States	Prospective	Yes	<ul style="list-style-type: none"> • 30% of 255 consecutive pts during a six-month period

¹Parenteral antibiotics only. pts, patients.

TABLE 2. DESCRIPTION AND RESULTS OF STUDIES THAT ASSESSED SYMPTOM RESPONSE FOLLOWING ANTIMICROBIAL USE AMONG PATIENTS RECEIVING PALLIATIVE OR HOSPICE CARE

Author (year)	n	Patient population	Included/excluded	Definition of symptom response	Results
Brabin & Allsopp (2008)	18 pts 20 infective episodes	209 pts in a palliative care unit	Included: All infection sites. Clinically diagnosed infection (does not include culture)	Record of symptomatic response to antibiotic treatment Based on clinical deterioration or improvement	<ul style="list-style-type: none"> Improved: 9/17 (52.9%), 95% CI = 27.8%–77.0%
Chen et al. (2002)	79 fevers treated w/ antibiotics	535 admits to palliative care/hospice unit	Included: All febrile episodes	Resolution of fever within three days of initial fever (>38.5°C)	<ul style="list-style-type: none"> Fever resolved: <ul style="list-style-type: none"> Antibiotic treated: 43/79 (54.4%), 95% CI = 42.8%–65.7% Not treated: 1/14 (7.1%), 95% CI = 0.2%–33.9%
Clayton et al. (2003)	41 pts 43 antibiotics courses	913 pts in a palliative care unit	Included: Clinical Dx of infection. Culture confirmation in 17/43 (40%) cases. All indications	Clinical assessment of helpful, unhelpful, or other Helpful: overall condition improved, if returned to prior functional status Unhelpful: symptoms/signs of infections didn't improve Other: unclear, unknown, or prophylactic administration	<ul style="list-style-type: none"> Helpful: 22/29 (75.9%), 95% CI = 56.5%–89.7%
Lam et al. (2005)	70 pts 120 infective episodes	87 cancer pts in a palliative care unit	Included: All indications meeting CDC definitions of specific infections Excluded: All indications not meeting CDC definitions of infections including febrile response; inflammation resulting from tissue response to injury or stimulation by noninfectious agents; and positive microbiological cultures not fulfilling CDC infection definition	Documented major symptom and examined physician notes to assess whether there was improvement	<ul style="list-style-type: none"> Improved: 47/120 (39.2%), 95% CI = 30.3%–48.5% Static: 61/120 (50.8%), 95% CI = 41.6%–60.1% Deteriorated: 12/120 (10.0%), 95% CI = 5.3%–16.8%
Mirhosseini et al. (2006)	26 pts 31 infective episodes	146 cancer pts in a tertiary palliative care unit	Included: All infection sites. Infection defined by clinical symptoms or cultures (54%)	-ESAS: change pre- to posttreatment, physician and patient rated (potentially rated by proxies, if patient became cognitively impaired) -Global assessment of pt condition by physician (improved, static, or deteriorated)	<ul style="list-style-type: none"> ESAS: all symptoms improved Patient rated: dysuria & "other" statistically significant Physician rated: cough statistically significant Global assessment: <ul style="list-style-type: none"> Improved: 15/31 (48.4%), 95% CI = 30.2%–66.9% Static: 4/31 (12.9%), 95% CI = 3.6%–29.8% Deteriorated: 2/31 (6.5%), 95% CI = 0.8%–21.4%

(continued)

TABLE 2. (CONTINUED)

Author (year)	n	Patient population	Included/excluded	Definition of symptom response	Results
Oh et al. (2006)	119 pts receiving antibiotics	141 cancer pts under palliative care in hospital	Included: fever > 38.3° C, elevated leukocytes. CRP elevation, positive blood culture	-Symptomatic improvement; examined charts—e.g., changes in yellowish sputum, dysuria, etc. -Resolution of fever (> 38.3° C)	<ul style="list-style-type: none"> • Symptom improvement: 18/84 (21.4%), 95% CI = 13.2%–31.7% (18 pts)¹ • Fever resolved: 47/98 (47.9%), 95% CI = 37.7%–58.3% (47 pts)
Reinbolt et al. (2005)	623 pts 633 infective episodes	1598 cancer pts in home-based hospice program	Included: Infection defined as presence of symptoms and physical signs interpreted by physician as an infection	Clinical improvement in ≥ 1 symptom associated with infection site—e.g., dysuria, fever, frequency pain associated with UTI—w/ in 72 hrs of starting antibiotics	<ul style="list-style-type: none"> • Overall—Improved: 359/633 (56.7%), 95% CI = 52.7%–60.6% • UTI—Improved: 210/265 (79.3%), 95% CI = 73.9%–84.0%; varied by antibiotic used, 60%–88% • Respiratory tract—Improved: 96/221 (43.4%), 95% CI = 36.8%–50.3%; varied by antibiotic used, 15%–53%
White et al. (2003)	117 pts 129 infective episodes	Cancer pts in home-based hospice program	Included: An infection was defined as the presence of symptoms and physical signs that were interpreted by the attending physician to have been caused by a microbial agent and documented as such in the patient's chart	Improvement in initial symptoms—fever, dyspnea, dysuria, pain	<ul style="list-style-type: none"> • UTI—Improved: 67%–92% (54 episodes); varied by antibiotics used • Respiratory tract—improved: 0%–50% (45 episodes)

¹35 patients removed from denominator because could not assess symptom changes. CDC, Centers for Disease Control and Prevention; CI, confidence interval; ESAS, Edmonton Symptom Assessment System; pts, patients; UTI, urinary tract infection.

In the prospective studies, symptom response was determined by clinician assessment, sometimes supplemented by patient or caregiver assessment.^{7,13,15,16}

Methods of assessing symptom response ranged from an ordinal scale to a validated metric.^{7,13} Clayton and colleagues used a rating of “helpful,” “unhelpful,” and “other,” which was specifically defined and based primarily upon resolution of infective symptoms.⁷ Mirhosseini and colleagues modified the Edmonton Symptom Assessment Scale, a validated metric for quantifying symptom intensity, to include symptoms of infection identified by patients and physicians.¹³ This study also used a physician’s “global assessment of the patient’s condition.”¹³

Efficacy of antimicrobial treatment

Improvement in the patient’s condition and/or infection-related symptoms (for all infection sites) following administration of antimicrobials by any route varied from 21.4%⁸ (95% CI, 13.2% to 31.7%) of cases to 56.7%¹⁵ (95% CI, 52.7% to 60.6%) of cases. Two studies, which included only parenteral antibiotic use, showed improvement in 52.9%⁶ (95% CI, 27.8% to 77.0%) and 75.9%⁷ (95% CI, 56.5% to 89.7%) of cases.

Three studies reported symptom response for specific infection sites.^{7,15,16} Of these, two studies reported symptomatic improvement of 60% to 92% for urinary tract infections (UTIs) and 0% to 53% for respiratory tract infections.^{15,16} There was no observed symptom improvement among patients with bacteremia.^{15,16} In both studies, antibiotics were administered orally except in bacteremia cases where parenteral administration was used.^{15,16} The third study, by Clayton and colleagues, also observed site-specific infections, but we determined that the proportions of patients whose symptoms improved were unreliable due to the inclusion of patients with unknown outcome status in the calculations.⁷

Studies including fever as an indication for antimicrobial use reported fever resolution in 47.9%⁸ (95% CI, 37.7% to 58.3%) and 54.4%⁹ (95% CI, 42.8% to 65.7%) of cases. In contrast, fever resolution occurred in 1 of 14 (7.1%) cases not treated with antimicrobial therapy.⁹

Discussion

We systematically reviewed the medical literature to summarize data regarding antimicrobial use for symptom management in palliative and hospice care. We identified eight studies that measured symptom improvement following antimicrobial therapy, but no study included a comparison group of patients not receiving antimicrobial therapy. Furthermore, heterogeneity in the measurement of both antimicrobial use and symptom reduction limit the utility of these data to clarify the benefits of antimicrobial therapy in this population.

The lack of comparison between patients who did and did not receive antimicrobial therapy is an important weakness of the existing literature, and as a result, we lack an accurate estimate of the effectiveness antimicrobial therapy. At present, there is not equipoise to consider a randomized study for this association. Rather, a cohort study comparing outcomes between patients with infective symptoms who received antimicrobial therapy to patients who did not receive antimicrobial therapy is possible and may address the weaknesses of previous studies. Furthermore, most studies utilized

subjective clinical notes to quantify or, more often, qualify patient symptoms rather than applying strict definitions of improvement or utilizing validated symptom measurement tools. Only one study used a validated method of symptom assessment, measured before and after initiation of antimicrobial therapy,¹³ and two studies used only resolution of fever as the criterion for improvement.^{8,9}

Clinical assessment of changes in symptom burden is highly subjective and is likely neither a sensitive nor specific method to identify infection-associated symptom improvement.¹⁷ In addition, it may not be possible to elucidate changes in infection-associated symptoms from other symptoms associated with the patient’s underlying disease trajectory. It is also possible that medications other than antimicrobial therapy administered to treat symptoms in these patients may mask the independent effect of antimicrobial therapy on infection-associated symptoms. However, these effects can be studied using validated measures of symptom burden and by adjustment for confounding variables. We did not identify a single study that adjusted for the potential confounding effects of underlying disease or other drug exposures in evaluating symptom improvement. These methodological limitations support the need for prospective studies using a systematic process and validated measures for assessing symptoms.

In addition to the lack of specificity to attribute symptoms to infectious causes, most infections in this patient population are not formally diagnosed, especially in hospice care.³ In our study of antibiotic prescribing in a nationwide sample of hospice patients in the last week of life, only 15% of patients who received antibiotics had a potential infectious indication documented in the patient’s medical chart.³ While our estimate and that of another recent study¹⁸ likely underrepresent the true frequency of suspected infections, they shed little light on the indications for antimicrobial use in this population. The Healthcare Infection Control Practices Advisory Committee (HICPAC) has proposed definitions for infections in home-based hospice care, but to our knowledge these have not been applied in research studies.¹⁹ In addition, Stone and colleagues recently updated definitions for infections in long-term care facilities.²⁰ It may be reasonable to consider these definitions or a similar approach when identifying suspected infections in residential hospice and palliative care populations. Furthermore, some infections, e.g., urinary tract infections or oral candidiasis may be more likely to improve symptomatically with antimicrobial therapy compared to other infections. In the studies that stratified results by infection site, greater improvement was observed in patients with urinary tract infections compared to other infection sites.^{7,15,16}

This study was limited by not including studies published in languages other than English. In addition, systematic reviews are susceptible to publication bias in that studies reporting a positive association between antimicrobial use and symptom reduction may be more likely to be submitted and accepted for publication compared to studies suggesting little or no benefit. We did not assess the potential for publication bias using funnel plots due to the limited number of studies identified. A recent review suggests that these assessments are not informative when the number of studies identified is less than 10.²¹

The results of this study reaffirm the need for high-quality research in this area. Specifically needed are prospective

studies that use robust measures of symptom improvement and account for important confounders such as concurrent symptom management strategies. Observational studies comparing patients who receive antimicrobial therapy with those who do not could employ propensity score matching to control for differences between the treated and untreated groups, especially confounding by indication. Finally, future studies need to be scrupulous about measuring adverse effects of antimicrobial therapy. Potential adverse events such as opportunistic *Clostridium difficile* infections and drug side effects are an important consideration when deciding to use antimicrobial therapy and may carry equal weight to any potential benefits of antimicrobial therapy in reducing symptom burden.

In conclusion, antimicrobial use is prevalent in hospice and palliative care patients, but existing research has not clarified the benefits of antimicrobial use for symptom improvement in this population. This study has identified the limitations of previous studies and presents opportunities for future research in this area. These studies are essential to improve the evidence base for the decision to use antimicrobial therapy and to assess the risks and benefits of this decision in this vulnerable population.

Acknowledgments

This work was supported by the Agency for Healthcare Research and Quality grant R36HS021068-01 (JSA) and National Institutes of Health grants KL2RR024141 (JCM), K07CA109511 (EKK), and K01AI071015-05 (JPF).

Author Disclosure Statement

The sponsors had no role in the design or conduct of the study; collection, management, analysis, or interpretation of the data; or preparation, review, or approval of the manuscript. JSA and JCM had no conflicts. EKK has received travel support from the California Health Care Foundation and support for educational presentations from The Kinsman Foundation. JPF has served as a consultant for Health Care Management Solutions, LLC and Easton Associates, LLC, and has received an unrestricted research grant from Merck & Co.

References

1. U.S. Census Bureau: *The Next Four Decades: The Older Population in the United States: 2010 to 2050 Population Estimates and Projections*. Washington, DC: U.S. Census Bureau. www.census.gov/prod/2010pubs/p25-1138.pdf.
2. NHPCO: *Facts and Figures: Hospice Care in America*. Alexandria, VA: National Hospice and Palliative Care Organization, 2012. www.nhpco.org/files/public/statistics_research/2011_facts_figures.pdf. (Last accessed November 9, 2012.)
3. Albrecht JS, McGregor JC, Fromme EK, Bearden DT, Furuno JP: A nationwide analysis of antibiotic use in hospice care in the final week of life. *J Pain Symptom Manage* 2013;46:483–490.
4. Ford PJ, Fraser TG, Davis MP, Kodish E: Anti-infective therapy at the end of life: Ethical decision-making in hospice-eligible patients. *Bioethics* 2005;19:379–392.
5. Nagy-Agren S, Haley H: Management of infections in palliative care patients with advanced cancer. *J Pain Symptom Manage* 2002;24:64–70.
6. Brabin E, Allsopp L: How effective are parenteral antibiotics in hospice patients? *Eur J Palliat Care* 2008;15:115–117.
7. Clayton J, Fardell B, Hutton-Potts J, Webb D, Chye R: Parenteral antibiotics in a palliative care unit: Prospective analysis of current practice. *Palliat Med* 2003;17:4–48.
8. Oh DY, Kim JH, Kim DW, et al.: Antibiotic use during the last days of life in cancer patients. *Eur J Cancer Care* 2006;15:74–79.
9. Chen LK, Chou YC, Hsu PS, et al.: Antibiotic prescription for fever episodes in hospice patients. *Support Care Cancer* 2002;10:538–541.
10. Chun ED, Rodgers PE, Vitale CA, Collins CD, Malani PN: Antimicrobial use among patients receiving palliative care consultation. *Am J Hosp Palliat Care* 2010;27:261–265.
11. Evers MM, Purohit D, Perl D, Khan K, Marin DB: Palliative and aggressive end-of-life care for patients with dementia. *Psychiatr Serv* 2002;53:609–613.
12. Lam PT, Chan KS, Tse CY, Leung MW: Retrospective analysis of antibiotic use and survival in advanced cancer patients with infections. *J Pain Symptom Manage* 2005;30:536–543.
13. Mirhosseini M, Oneschuk D, Hunter B, Hanson J, Quan H, Amigo P: The role of antibiotics in the management of infection-related symptoms in advanced cancer patients. *J Palliat Care* 2006;22:69–74.
14. Oneschuk D, Fainsinger R, Demoissac D: Antibiotic use in the last week of life in three different palliative care settings. *J Palliat Care* 2002;18:25–28.
15. Reinbolt RE, Shenk AM, White PH, Navari RM: Symptomatic treatment of infections in patients with advanced cancer receiving hospice care. *J Pain Symptom Manage* 2005;30:175–182.
16. White PH, Kuhlenschmidt HL, Vancura BG, Navari RM: Antimicrobial use in patients with advanced cancer receiving hospice care. *J Pain Symptom Manage* 2003;25:438–443.
17. Fromme EK, Eilers KM, Mori M, Hsieh YC, Beer TM: How accurate is clinician reporting of chemotherapy adverse effects? A comparison with patient-reported symptoms from the quality-of-life questionnaire C30. *J Clin Oncol* 2004;22:3485–3490.
18. Dwyer LL, Harris-Kojetin LD, Valverde RH, et al.: Infections in long-term care populations in the United States. *J Am Geriatr Soc* 2013;61:342–349.
19. Embry FC, Chinnes LF: *APIC-HICPAC Surveillance Definitions for Home Health Care and Home Hospice Infections*. www.premierinc.com/safety/topics/guidelines/downloads/Definitions-home-health-hospice.pdf. (Last accessed April 1, 2013.)
20. Stone ND, Ashraf MS, Calder J, et al.: Surveillance definitions of infections in long-term care facilities: Revisiting the McGeer criteria. *Infect Control Hosp Epidemiol* 2012;33:965–977.
21. Sterne JA, Sutton AJ, Ioannidis JP, et al.: Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ* 2011;343:d4002.

Address correspondence to:
 Jon P. Furuno, PhD
 OSU/OHSU College of Pharmacy
 Department of Pharmacy Practice
 3303 SW Bond Avenue
 Mail Code: CH12C
 Portland, OR 97239

E-mail: furuno@ohsu.edu