Prevention of Infection

A systematic review of evidence-based practice interventions for management in patients with cancer

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BACKGROUND: Cancer-related infections lead to increases in mortality, antibiotic use, and hospital stays. Other adverse outcomes include dose delays and reductions, which can result in suboptimal treatment outcomes.

OBJECTIVES: Effective implementation of risk assessment and evidence-based interventions for the prevention and treatment of infection are essential to improve care and reduce costs related to infections in patients with cancer receiving immunosuppressive therapy.

METHODS: The Oncology Nursing Society (ONS) Putting Evidence Into Practice (PEP) prevention of infection resource have been developed and updated to identify and disseminate the best available scientific evidence.

FINDINGS: Pharmacologic and nonpharmacologic interventions were evaluated, resulting in recommended for practice rating for catheter care bundles, antimicrobial prophylaxis, vaccination for specific populations, and implementation of contact precautions for resistant organisms.

KEYWORDS
cancer-related infection; evidence-based practice; prevention of infection; PEP

CANCER-RELATED INFECTIONS CAUSE SIGNIFICANT COMPLICATIONS in cancer care, affecting patient morbidity and mortality (Brand et al., 2016; Chindaprasirt et al., 2013; Kuderer, Dale, Crawford, Cosler, & Lyman, 2006; Lyman et al., 2010). Patients with cancer are at risk for viral, bacterial, and fungal infections (National Comprehensive Cancer Network [NCCN], 2017b). Immunosuppression related to nature of the malignancy, chemotherapy, or targeted therapies increases infection risk (Gudiol, Aguado, & Carratalà, 2016; Ibrahim et al., 2013). Infections can cause dose delays and dose reductions that prevent optimal treatment outcomes (Bilir et al., 2016; Gafter-Gvili & Polliack, 2016; Lyman et al., 2010; Weycker et al., 2015).

A high infection risk is predictive of higher mortality rates, longer hospitalization, and higher cost of care (Wang, Lopez, & Chan, 2015; Weycker et al., 2015). Age older than 65 years is associated with a higher incidence of infections during treatment (American Cancer Society [ACS], 2016; Cooksley, Avritscher, Rolston, & Elting, 2009; Grosso et al., 2012; Zanussi, Serraino, Dolcetti, Berretta, & De Paoli, 2013), and 87% of people diagnosed with cancer in the United States are aged 50 years or older (ACS, 2017).

Patients with cancer have the potential for recurring infections requiring various antimicrobial treatment and prophylaxis. A systemic review evaluating trends in epidemiology and antibiotic resistance for bacteremia in these patients revealed that gram-negative bacteria was the most frequent isolate, with substantial emergence of antimicrobial-resistant strains in both gram-negative and gram-positive bacteria (Montassier, Batard, Gastinne, Potel, & de La Cochetière, 2013). Management of cancer-related infections related to multi-drug resistant organisms present challenges, including limited effective antibiotic choices, and are associated with higher risks for morbidity and mortality (Gudiol & Carratalà, 2014). Epidemiologic trends for emerging resistant strains of pathogens in patients with cancer can threaten antimicrobial resistance in the larger populations (Gudiol & Carratalà, 2014; Gudiol et al., 2016; Kalantar et al., 2015; Liu et al., 2016; Satlin et al., 2016). The economic burden from resistant pathogens is related to duration of illness, expensive antimicrobials, and additional diagnostics (Magauran & Salgado, 2011).
Sepsis has a high fatality rate in patients with cancer (Gudiol et al., 2016; Marin et al., 2014; Marin, Gudiol, García-Vidal, Ardanuy, & Carratalà, 2014; Satlin et al., 2016). One study reports mortality from *Staphylococcus aureus* central line–associated bloodstream infections of 25%–30% in patients with cancer (El Zakhem et al., 2014). A retrospective cohort study of patients with metastatic solid tumors (N = 15,318) investigated rates of febrile neutropenia (FN), its associated risks, and consequences (Weycker et al., 2015). The study used data repositories from geographically diverse private healthcare claims from 2006–2011. Depending on cancer type, the rate of FN ranged from 13%–21%, with costs per inpatient episode ranging from $16,000–$19,000.

**Prevention of Infection**

The Oncology Nursing Society (ONS) Putting Evidence Into Practice (PEP) resources have been developed to identify and disseminate the best available scientific evidence supporting best practices to improve nurse-sensitive patient outcomes (Johnson, 2014). The PEP prevention of infection resource is a comprehensive synthesis of currently published nursing and medical research literature summarizing and classifying evidence by weight for effectiveness in specific patient outcomes (Johnson, 2014). This article provides an update on the PEP prevention of infection team’s evidence review, offering a summary of recommendations for best infection prevention practices for nurses caring for adult patients with cancer.

**Risk Assessment**

Three risk assessments—risk for infection, risk for cancer-related FN, and risk for FN complications—have been developed to support early identification and intervention of cancer-related infections. Additional assessments specific to autologous and allogeneic hematopoietic cell transplantation (HCT) are also available (NCCN, 2017b; Tomblyn et al., 2009).

**INFECTION:** Patients undergoing systemic cancer treatment should be evaluated using patient and treatment factors for infection risk prior to each treatment, including the first cycle. Patients are categorized as high risk for infection if their treatment includes autologous HCT, induction or consolidation for acute leukemia, or a alemtuzumab-containing regimen. Therapy that requires high-dose steroids to treat graft-versus-host disease (GVHD) or neutropenia expected to last more than 10 days also places patients at high risk for infection. Intermediate risk for infection includes diagnosis of multiple myeloma, lymphoma or chronic lymphocytic leukemia, treatment with autologous HCT, a purine analog–containing regimen, or one that results in neutropenia with expected duration of 7–10 days. The risk for infection is low if the patient is receiving standard chemotherapy doses and neutropenia is expected to last less than seven days (NCCN, 2017b). **FEBRILE NEUTROPENIA:** Guidelines from the NCCN, the EORTC, the American Society of Clinical Oncology (ASCO), and the Infectious Diseases Society of America (IDSA) identify fever in the presence of neutropenia as an increased risk for infection. FN is defined as fever with an oral temperature of 38.3ºC or greater or a single temperature of 38ºC or greater and lasting more than one hour; neutropenia is defined as 500 neutrophils or less per mcl or less than 1,000 neutrophils per mcl trending down and predicted to fall below 500 per mcl within 48 hours. Figure 1 categorizes risk factors for developing FN.

**FIGURE 1.**

**RISK FACTORS FOR DEVELOPING FEBRILE NEUTROPENIA**

**DISEASE-RELATED FACTORS**
- Disease in advanced stage
- Any previous, preexisting, or prolonged neutropenia
- Leukemia, lymphomas, myelodysplastic syndrome
- Primary cancer of breast, lung, colon/rectum, or ovary

**PATIENT-RELATED FACTORS**
- Age older than 65 years
- Female gender
- Recent surgery
- Open wounds
- Preexisting infection
- Decreased neutrophil count at start of treatment cycle
- Renal or liver dysfunction
- Poor performance status
- Poor nutritional status

**TREATMENT-RELATED FACTORS**
- Chemotherapy intensity, including dose dense, high dose, or myeloablative regimens
- Immunosuppressive medications
- Target relative dose intensity of 85% or greater
- Curative treatment intent
- Previous myelosuppressive radiation or chemotherapy

Note. Based on information from National Comprehensive Cancer Network, 2017b.
**FEVER NEUTROPENIA COMPLICATIONS:** Using a comprehensive patient, disease, and treatment risk assessment results in patients being stratified as high risk for developing complications of FN if they present with any of the following:

- **A Multinational Association for Supportive Care in Cancer** score lower than 21 (Baskaran, Gan, & Adeeba, 2008)
- Inpatient status when fever starts
- Clinically unstable
- Major comorbidity or comorbidities
- Allogeneic HCT
- Treated with alemtuzumab
- A neutropenia count of 100 cells per mcl or less that is expected to last seven days or longer
- Liver dysfunction with aminotransferases of five times the upper limit of normal
- Renal disease with creatinine clearance of less than 30 ml per minute
- Cancer that is progressing or uncontrolled
- Complex infections, including pneumonia
- Grade 3–4 mucositis

Patients are categorized as low risk if they do not have any of the high-risk factors (NCCN, 2017b). NCCN stratifies the risk as high when the associated risk is greater than 20%, moderate when the risk is 10%–20%, or low if the risk is less than 10% for FN. The assessment should be completed before the initial treatment and each subsequent treatment (Aapro et al., 2011; NCCN, 2017a, 2017b).

The Multinational Association for Supportive Care in Cancer scoring system includes the patient’s burden of illness, comorbidities, characteristics of malignancy, age, and level of hydration. A calculator for scoring is available at http://bit.ly/2EnYm3G.

**Assessing Infection Risk in Hematopoietic Stem Cell Transplantation**

Patients undergoing HCT have additional risks for opportunistic infections. Differences in risk for infectious complications are noted between recipients of autologous versus allogeneic transplantation (NCCN, 2017b; Tomblin et al., 2009). The loss of mucosal integrity from myeloablative therapy prior to autologous HCT is a risk factor for developing bacteremia (Sonis et al., 2001). An inverse relationship between response to granulocyte-colony-stimulating factor (G-CSF) and incidence of infection (p < 0.01) was also a reliable predictor for autologous HCT-related infection risk (Straka et al., 2011).

For patients undergoing allogeneic HCT, the risk for infection is specific to phase of engraftment (Sonis et al., 2001; Tomblin et al., 2009). During the pre-engraftment phase (about 0–30 days after allogeneic HCT), the risk for fungal and bacterial infections is related to neutropenia and interruption of mucosal integrity. Patients are at risk and should be assessed for reactivation of herpes simplex virus (HSV). The post-engraftment phase (30–100 days after HCT) places the patient at risk for herpes viruses, cytomegalovirus (CMV), *Pneumocystis jiroveci* pneumonia (PCP), and *Aspergillus*. Beyond 100 days, patients continue to be at risk for CMV, varicella zoster virus (VZV), and *Streptococcus pneumoniae* or other encapsulated bacteria (NCCN, 2017b; Ullmann et al., 2016).

**Methods**

An extensive literature search was performed of PubMed and CINAHL® for research articles, systematic reviews, guidelines, and meta-analyses published in English. This update includes studies retrieved from January 2009 to January 2017, in addition to 31 articles published prior to 2009 that were included in previous reviews. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) diagram is shown in Figure 2. Abstracts, proceedings, letters to the editor, grey literature, descriptive studies, and case reports were excluded. Research that did not report on interventions to prevent infection of FN or did not include patients with cancer were excluded. The search strategy, search terms, databases, and inclusion criteria are found at www.onc.org/content/prevention-infection-search-strategy. Inclusion criteria have evolved in response to the quality and amount of evidence. As of January 2016, additional inclusion criteria were added, including (a) sample size must have been at least 40, or 20 per study group, and (b) complex interventions must have been described with sufficient detail to identify the components of the intervention.

**FIGURE 2.**

**PRISMA DIAGRAM OF SEARCH STRATEGY**

Articles included in past reviews (n = 31)

Total articles identified through database searching and monthly automatic alerts, from January 2009 to January 2017 (n = 3,794)

- PubMed (n = 3,294)
- CINAHL® (n = 500)

Studies selected after initial review (removal of duplicates and those that did not meet inclusion criteria) (n = 455)

Additional studies removed following full-text review and additional studies included that were identified through other sources. Final studies included for full review (N = 275)

PRISMA—Preferred Reporting Items for Systematic Reviews and Meta-Analyses
The 273 articles meeting inclusion criteria were divided into two categories: (a) prevention of infection: general and (b) prevention of infection: transplant. Each article was reviewed by a member of the ONS PEP prevention of infection team. This review and article were then reviewed by a second team member. Following that, the entire PEP prevention of infection team discussed the reviews to confirm that articles were appropriate for inclusion and that review summaries accurately represented the content (Mitchell & Friese, 2009; Ropka & Spencer-Cisek, 2001) (see Table 1).

Evidence Review
This section describes evidence-based interventions for prevention of infection. Efficacy and recommended timing for interventions are included for pharmacologic and nonpharmacologic interventions (see Table 2). Separate considerations are noted for patients undergoing hematopoietic stem cell transplantation.

Interventions to Prevent Infection

**COLONY-STIMULATING FACTORS:** CSFs are a class of biologic agents that regulate the growth and development of neutrophils and are indicated to decrease the neutropenic complications of myelosuppressive chemotherapy and to maintain chemotherapy dose intensity. CSFs decrease the severity and duration of neutropenia and incidence of FN, infection, infection-related mortality, and all-cause mortality in adults and children receiving cancer chemotherapy (Kuderer, 2011; Lyman et al., 2010).

NCCN, ASCO, EORTC, the European Society for Medical Oncology, and the National Institute for Health and Care Excellence are uniform in their recommendation of primary prophylaxis of a CSF for patients undergoing chemotherapy that has a 20% or higher risk of FN (Aapro et al., 2011; Crawford, Caserta, & Roila, 2010; NCCN, 2017a; Phillips et al., 2012; Smith et al., 2015).

CSFs should also be considered for individuals undergoing chemotherapy who have less than a 20% risk for FN if they have other risk factors for neutropenia. The most important risk factor is age older than 65 years. Other risk factors include prior extensive chemotherapy or radiation, comorbid conditions, renal or hepatic dysfunction, HIV infection, performance status, bone marrow involvement, and pretreatment blood counts (NCCN, 2017a; Smith et al., 2015).

Filgrastim, filgrastim-sndz, tbo-filgrastim, and pegfilgrastim are FDA-approved CSFs indicated to prevent chemotherapy-induced neutropenia. Filgrastim, filgrastim-sndz, and tbo-filgrastim are biologically similar G-CSFs that have equivalent clinical activity.

### Table 1. Putting Evidence into Practice Weight-of-Evidence Classification Schema

<table>
<thead>
<tr>
<th>Weight-of-Evidence Category</th>
<th>Description</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Recommended for practice</td>
<td>Effectiveness is demonstrated by strong evidence from rigorously designed studies, meta-analyses, or systematic reviews. Expected benefit exceeds expected harms.</td>
<td>At least two multisite, well-conducted, randomized, controlled trials (RCTs) with at least 100 participants</td>
</tr>
<tr>
<td>Likely to be effective</td>
<td>Evidence is less well established for those listed under recommended for practice.</td>
<td>One well-conducted RCT with less than 100 participants or at one or more study sites</td>
</tr>
<tr>
<td>Benefits balanced with harms</td>
<td>Clinicians and patients should weigh the beneficial and harmful effects according to individual circumstances and priorities.</td>
<td>RCTs, meta-analyses, or systematic reviews with documented adverse effects in certain populations</td>
</tr>
<tr>
<td>Effectiveness not established</td>
<td>Data currently are insufficient or are of inadequate quality.</td>
<td>Well-conducted case control study or poorly controlled RCT</td>
</tr>
<tr>
<td>Effectiveness unlikely</td>
<td>Lack of effectiveness is less well established compared to those listed under not recommended for practice.</td>
<td>Single RCT with at least 100 participants that showed no benefit</td>
</tr>
<tr>
<td>Not recommended for practice</td>
<td>Ineffectiveness or harm clearly is demonstrated, or cost or burden exceeds potential benefit.</td>
<td>No benefit or excess costs or burden from at least two multisite, well-conducted RCTs with at least 100 participants</td>
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Note. Based on information from Mitchell & Friese, 2009.
(NCCN, 2017a; Smith et al., 2015). Filgrastim, filgrastim-sndz, and tbo-filgrastim are subcutaneous injections administered daily after each cycle of chemotherapy until neutrophil recovery. Pegfilgrastim, a pegylated formulation of filgrastim, is a subcutaneous injection administered once after each cycle of chemotherapy. The major adverse effect of CSF use is bone pain (NCCN, 2017a).

Recommended timing for administration of CSFs is between 1 and 3–4 days after chemotherapy (NCCN, 2017a; Smith et al., 2015). A meta-analysis of patients with non-Hodgkin lymphoma and breast cancer undergoing chemotherapy who were treated with same-day versus next-day pegfilgrastim showed a trend toward increased grade 4 neutropenia in the group of patients who received pegfilgrastim on the same day as chemotherapy (Burris et al., 2010). Other studies showed an increased risk of neutropenia (Li et al., 2016) and FN (Weycker et al., 2015) when CSFs were administered on the same day of chemotherapy instead of day 2 or beyond. The biologic basis for this observation may be that stimulating myeloid progenitor cell growth may render them more vulnerable to destruction by cytotoxic chemotherapy.

**ANTIBIOTIC PROPHYLAXIS:** For purposes of this PEP update, antibiotic prophylaxis in clinical oncology care is defined as antibiotics prescribed for patients undergoing chemotherapy to decrease the risk of infection during chemotherapy-induced neutropenia. A meta-analysis of 109 trials with 13,579 participants showed that the use of fluoroquinolones for prophylaxis during chemotherapy-induced neutropenia resulted in significant reduction in the risk for all-cause mortality (RR = 0.66, 95% CI [0.55, 0.79], p < 0.000001) and infection-related mortality (RR = 0.61, 95% CI [0.48, 0.77], p = 0.04), as well as decreased incidence of fever, documented infection, and bacteremia (Gafter-Gvili et al., 2012). No significant differences in outcomes were noted between various antibiotic regimens, although the greatest effect was seen with quinolones. A majority of patients in this review had hematologic malignancies, which rendered them at high risk for infection.

Because prophylactic antibiotics may promote antibiotic resistance, their use should be limited to high-risk patients. Guidelines for NCCN, ASCO, and IDSA advise against antibiotic prophylaxis unless profound neutropenia (absolute neutrophil count less than 100) is expected to exceed 7–10 days, such as after high-dose chemotherapy, acute leukemia regimens, or HCT regimens (Freifeld et al., 2011; NCCN, 2017b).

**ANTIFUNGAL PROPHYLAXIS:** Routine antifungal prophylaxis is not recommended for patients with an anticipated duration of neutropenia of less than 7–10 days (Freifeld et al., 2011; NCCN, 2017b). Antifungal prophylaxis should be reserved for a targeted group of high-risk patients, such as those with acute lymphoblastic leukemia and those with acute myeloid leukemia or myelodysplastic syndrome during neutropenia (NCCN, 2017b).

Meta-analyses have demonstrated that antifungal prophylaxis decreases the risk of invasive fungal infections (IFI) and mortality in high-risk patients with hematologic malignancies (Zhao et al., 2015; Ziakas, Kourbeti, Voulgarelis, & Mylonakis, 2010). Posaconazole is the preferred agent to prevent IFI in patients with acute myelogenous leukemia or myelodysplastic syndrome undergoing induction chemotherapy (Cornely et al., 2009; NCCN, 2017b; Tacke et al., 2014). In three Cochrane reviews of antifungal prophylaxias (that did not include posaconazole), amphotericin B, ketoconazole, fluconazole, and voriconazole were all effective prophylaxis (Gøtzsche & Johansen, 2014; Johansen & Gøtzsche, 2014; Jørgensen, Gøtzsche, Dalbøge, & Johansen, 2014).

**PNEUMOCYSTIS JIROVECCI PNEUMONIA PROPHYLAXIS:** Patients at risk for *Pneumocystis pneumonia* (from PCP) are those undergoing treatment for acute lymphocytic leukemia, receiving alemtuzumab or idelisib, receiving temozolomide with radiation therapy, or being treated with the prednisone equivalent of 20 mg or more for four or more weeks (NCCN, 2017b). Trimethoprim-sulfamethoxazole (TMP/SMX) is the preferred agent for prophylaxis.

**ANTIVIRAL PROPHYLAXIS FOR AT-RISK PATIENTS:** Prophylactic treatment with antiviral agents is not recommended routinely for all patients receiving cancer treatment. Antiviral prophylaxis is recommended for patients with solid tumors who have had a prior episode of HSV; patients with acute leukemia, lymphoma, multiple myeloma, or chronic lymphocytic leukemia; and patients receiving purine analog therapy or alemtuzumab (NCCN, 2017b). Patients receiving proteasome inhibitors (e.g., bortezomib) are at high risk of VZV reactivation, and VZV prophylaxis is recommended. Patients receiving alemtuzumab are at risk for CMV reactivation, and CMV surveillance is recommended. Patients should be screened for hepatitis B, and prophylaxis is recommended for chronic hepatitis B carriers.

**Vaccinations**

Annual influenza vaccination is recommended by the Centers for Disease Control and Prevention’s Advisory Committee on Immunization Practices (ACIP), the NCCN, and the IDSA for patients, their close contacts, and healthcare workers in close contact with these patients (Kroger, Duchin, & Vázquez, 2017; NCCN, 2017b; Rubin et al., 2014). Annual influenza vaccination is not recommended for patients who have been treated with anti-B cell antibodies within the previous six months or those receiving intensive chemotherapy as induction or consolidation for acute leukemia (Kroger, Duchin, & Vázquez, 2017; NCCN, 2017b, Rubin et al., 2014).
et al., 2014). No clear consensus has been reached on the most appropriate timing of vaccination; optimally, vaccination should be given more than two weeks from the time of immunosuppression (Rubin et al., 2014).

The conjugate pneumococcal vaccine PCV13 should be administered to patients who have not previously been vaccinated (Kroger et al., 2017; NCCN, 2017b, Rubin et al., 2014). The polysaccharide pneumococcal vaccine PPSV23 should be...

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<tr>
<th>TABLE 2. PREVENTION OF INFECTION INTERVENTIONS AND LEVELS OF EVIDENCE</th>
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<tr>
<td><strong>CATEGORY</strong></td>
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| **Recommended for practice** | - Antibiotic prophylaxis in at-risk patients  
- Antifungal prophylaxis in at-risk patients  
- CSFs, including biosimilars in at-risk patients  
- Hand hygiene (with alcohol sanitizer)  
- Contact precautions for resistant organisms  
- Antiviral prophylaxis for select at-risk patients  
- Influenza vaccination  
- Pneumococcal and meningococcal vaccination  
- Adherence to general infection control recommendations  
- Catheter care bundle for prevention of CLABSI  
- Environmental interventions  
- Chlorhexidine skin prep | - Antibiotic prophylaxis in at-risk patients  
- Antifungal prophylaxis in at-risk patients  
- CSFs, including biosimilars in at-risk patients  
- Hand hygiene (with alcohol sanitizer)  
- Contact precautions for resistant organisms  
- Antiviral prophylaxis for select at-risk patients  
- Influenza vaccination  
- Pneumococcal and meningococcal vaccination  
- Adherence to general infection control recommendations  
- Catheter care bundle for prevention of CLABSI  
- Environmental interventions  
- Chlorhexidine skin prep |
| **Likely to be effective** | - Preconstruction planning  
- Antimicrobial-coated central venous catheters in adults  
- Antibiotic abdominal lavage in colorectal surgery  
- Chlorhexidine-impregnated washcloths and/or bath  
- Preoperative antibiotics  
- Institutional initiatives  
- Positive expiratory pressure and self-monitoring | - Chlorhexidine-impregnated washcloths and/or bath  
- Institutional initiatives |
| **Benefits balanced with harms** | - IV immunoglobulin | - IV immunoglobulin |
| **Effectiveness not established** | - Acupuncture/ electroacupuncture  
- Antibiotic-coated sutures  
- Antimicrobial catheter lock  
- Antimicrobial-impregnated IV catheters in pediatric patients  
- Berbamine  
- Chlorhexidine sponge dressing  
- G-CSF and GM-CSF alteration in schedule  
- Cranberry juice  
- Disinfecting IV catheter caps  
- Drain antisepsis  
- Garlic  
- Honey  
- Mistletoe extract  
- Needleless IV system  
- Omega 3 fatty acids  
- Preoperative care bundle  
- Probiotics  
- Protective isolation  
- Silver-impregnated dressing  
- Staff training  
- Urokinase IV catheter flush | - Antimicrobial-coated central venous catheters  
- Disinfecting IV catheter caps  
- Granulocyte transfusions  
- Palifermin  
- Protective isolation  
- Staff training  
- Urokinase IV catheter flush |
| **Effectiveness unlikely** | - Low microbial diet/restriction of fresh fruits and vegetables  
- CSF by IV route rather than subcutaneous route  
- Frequent IV tubing component changes | - Restriction of fresh fruits and vegetables  
- Frequent IV tubing component changes |
| **Not recommended for practice** | - Implantable gentamicin sponge  
- Use of live attenuated vaccines  
- Extended postoperative antibiotics | - Use of live attenuated vaccines |

CLABSI—central line–associated bloodstream infections; CSF—colony-stimulating factor; G-CSF—granulocyte–colony-stimulating factor; GM-CSF—granulocyte macrophage–colony-stimulating factor

Note. Based on information from Oncology Nursing Society, 2017a, 2017b.
administered eight weeks later and repeated every five years. Patients previously vaccinated with PPSV23 only should be vaccinated with PCV13 at least one year after their last PPSV23 dose. The meningococcal vaccine is recommended for patients with complement deficiencies or who receive eculizumab. Patients who require splenectomy or who have functional asplenia should receive pneumococcal, meningococcal, and *Haemophilus influenzae* b conjugate (NCCN, 2017b).

Live vaccinations should not be administered to patients undergoing chemotherapy or immunosuppressive therapy (Kroger et al., 2017; NCCN, 2017b; Rubin et al., 2014). Most patients can return to usual vaccination schedule and receive live vaccinations starting three months following chemotherapy or six months following treatment with anti-B cell antibodies (Rubin et al., 2014).

**Pharmacologic Interventions for Patients Undergoing Hematopoietic Stem Cell Transplantation**

**COLONY-STIMULATING FACTORS:** No consensus exists on the use of CSFs following autologous or allogeneic transplantation (NCCN, 2017a). CSF use may accelerate neutrophil recovery, but it has not been established that CSFs decrease the risk of infection or mortality (NCCN, 2017a). If CSFs are used, pegfilgrastim and filgrastim appear to be equally effective (Ziakas & Kourbeti, 2012).

**ANTIBIOTIC PROPHYLAXIS:** Fluoroquinolone prophylaxis is recommended by several professional guidelines for all patients undergoing HCT throughout the period from conditioning to engraftment (Freifeld et al., 2011; NCCN, 2017b; Tomblyn et al., 2009). The NCCN and IDSA both recommend levofloxacin in situations with increased risk for oral mucositis-related viridans streptococci infections (Freifeld et al., 2011; NCCN, 2017b). Patients undergoing allogeneic HCT are at increased risk of pneumococcal infection. Penicillin prophylaxis is recommended starting three months following allogeneic HCT until one year after transplantation or until immunosuppression for chronic GVHD is discontinued (NCCN, 2017b).

**ANTIFUNGAL PROPHYLAXIS:** Antifungal prophylaxis is recommended for high-risk patients undergoing HCT, including patients with allogeneic HCT with neutropenia, autologous HCT with mucositis, and patients with GVHD (Freifeld et al., 2011; Majhail et al., 2012; NCCN, 2017b; Tomblyn et al., 2009; Weissinger et al., 2012). Fluconazole is recommended to prevent IFI in patients undergoing allogeneic HCT with severe GVHD (NCCN, 2017b; Ullmann et al., 2007). Fluconazole is recommended to prevent IFI in patients undergoing allogeneic HCT until the development of GVHD (Cornely et al., 2009). Posaconazole is recommended to prevent IFI in allogeneic HCT recipients with severe GVHD (NCCN, 2017b; Ullmann et al., 2007).

**ANTIVIRAL PROPHYLAXIS:** HSV and VZV prophylaxis are recommended for patients undergoing autologous and allogeneic HCT and patients with GVHD (Freifeld et al., 2011; Tomblyn et al., 2009). VZV prophylaxis should continue for at least one year following allogeneic HCT and for 6–12 months following autologous HCT (NCCN, 2017b). Options for antiviral prophylaxis include acyclovir, famciclovir, and valaciclovir. The doses for VZV prophylaxis are higher than for HSV prophylaxis (NCCN, 2017b).

For patients who are CMV seropositive, surveillance should continue for 1–6 months following allogeneic HCT or longer if patients are on immunosuppression for GVHD (NCCN, 2017b).

**PNEUMOCYSTIS JIROVECCI PNEUMONIA PROPHYLAXIS:** Prophylaxis against PCP with TMP/SMX is recommended for at least six months after allogeneic HCT and longer if the patient continues to be immunosuppressed (NCCN, 2017b; Tomblyn et al., 2009). NCCN (2017b) also recommends consideration of TMP-SMX prophylaxis for 3–6 months in patients who have had autologous HCT (NCCN, 2017b). Pentamidine, atovaquone, and dapsone can be used for PCP prophylaxis in patients intolerant to TMP-SMX (NCCN, 2017b).

**Vaccination for Patients Undergoing Hematopoietic Stem Cell Transplantation and Their Close Contacts**

Annual vaccination against influenza is recommended for transplantation recipients, their close contacts, and healthcare providers caring for patients undergoing HCT (Freifeld et al., 2011; Majhail et al., 2012; NCCN, 2017b; Tomblyn et al., 2009). Vaccination should occur at least two weeks prior to immunosuppressive therapy (NCCN, 2017b). The NCCN and American Society for Blood and Marrow Transplantation issued a schedule of recommended vaccines for post-transplantation patients. The inactivated vaccines diphtheria/tetanus/acellular pertussis, *haemophilus influenzae* type b, pneumococcal, hepatitis A, hepatitis B, meningococcal, and inactivated polio vaccine are recommended 6–12 months following autologous or allogeneic transplantation. The live vaccines measles/mumps/rubella and VZV are not recommended unless the patient is seronegative and is more than two years following transplantation and not on immunosuppression (NCCN, 2017b; Tomblyn et al., 2009).

**Nonpharmacologic Interventions for Prevention of Infection in the General and Transplantation Populations**

**CENTRAL VENOUS CATHETER CARE AND BUNDLES:** Central venous catheter care and care bundles were developed to reduce the number of central line infections and standardize central...
line care practices (Bundy et al., 2014). Guidelines provide recommendations for education and training of staff, hand hygiene, sterile techniques, dressing regimens, antimicrobial-impregnated catheters for long-term catheter use, and site cleaning (O’Grady et al., 2011). Every person who enters the room during the insertion or access of the line should perform hand hygiene according to standard recommendations (Schiffer et al., 2013). The skin at the insertion site should be scrubbed with 2% chlorhexidine for 30 seconds and should be allowed to dry for at least 30 seconds when inserting or accessing the central line (Schiffer et al., 2013). There is no evidence that particular dressing types or more frequent IV set and/or dressing changes decrease the risk of infection, and, in fact, frequent IV or dressing changes may actually increase risk of infection. The use of topical antibiotic ointment or cream at the insertion site is not recommended because of the potential for increased fungal infections and antibiotic resistance (Schiffer et al., 2013). Transparent dressings on long-term central lines should be changed at least every seven days or when the patient is diaphoretic, the catheter site is oozing, or the catheter dressing looks damp loosened or visibly soiled (O’Grady et al., 2011). Insertion sites should be monitored visually when changing the dressing or by palpation through an intact dressing on a regular basis, depending on the clinical situation of the patient. If there is any tenderness at the site, fever without obvious source, or other symptoms suggesting bloodstream or localized infection the dressing should be removed and the site thoroughly examined (O’Grady et al., 2011). The use of antimicrobial-impregnated CLs remains somewhat controversial because of cost (Schiffer et al., 2013). These guidelines and use of catheter care bundles have decreased central line-associated bloodstream infections in pediatric, general oncology, and transplantation populations (Bundy et al., 2014; O’Grady et al., 2011; Schiffer et al., 2013).

CHLORHEXIDINE SKIN PREPARATION: According to the ASCO guidelines for catheter care, chlorhexidine-based preparations used at the time of insertion result in a decrease in the incidence of CVC-related infections by 40%–50% compared with povidone-iodine solutions (Schiffer et al., 2013). A chlorhexidine-impregnated dressing at the insertion site also substantially reduces the risk of CVC or exit-site bacterial colonization (14.8% versus 26.9%; odds ratio [OR] = 0.47; p < 0.001) (Schiffer et al., 2013). In studies of effectiveness of chlorhexidine, an antiseptic solution used to clean the skin prior to invasive procedures was found to be equally or more effective than 70% alcohol solution, 10% povidone-iodine solution, 0.025% benzalkonium chloride, and 4% benzyl alcohol (O’Grady et al., 2011).

Contact Precautions for Resistant Organisms
Contact precautions, including donning gowns and gloves to enter the room, have been recommended in patients with resistant organisms. Studies have shown a decrease in the incidence of drug-resistant organisms, including methicillin-resistant Staphylococcus aureus and vancomycin-resistant Enterococcus when full-contact precautions are taken, including patient isolation, wearing of gowns and gloves with proper disposal, and use

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FIGURE 3.
PATIENT EDUCATION RESOURCES FOR PREVENTION OF INFECTION

AMERICAN CANCER SOCIETY

CENTERS FOR DISEASE CONTROL AND PREVENTION
http://bit.ly/2zcj1fI

NATIONAL COMPREHENSIVE CANCER NETWORK

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

FIGURE 4.
CLINICAL PRACTICE RESOURCES FOR PREVENTION OF INFECTION

AMERICAN NURSES ASSOCIATION
Recommendations on the role of RNs in hospital antibiotic stewardship

AMERICAN SOCIETY OF CLINICAL ONCOLOGY
Clinical practice guideline update

CENTERS FOR DISEASE CONTROL AND PREVENTION
General best practice guidelines for immunization
www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html

EUROPEAN SOCIETY FOR MEDICAL ONCOLOGY
Clinical practice guidelines

INFECTIOUS DISEASES SOCIETY OF AMERICA
Immunizations and vaccine policy

MULTINATIONAL ASSOCIATION OF SUPPORTIVE CARE IN CANCER
Febrile neutropenia risk calculator
http://bit.ly/2CE0nwG

NATIONAL COMPREHENSIVE CANCER NETWORK
Clinical practice guidelines for infections and myeloid growth factors
http://bit.ly/2qOQwA

ONCOLOGY NURSING SOCIETY
Putting Evidence Into Practice
www.ons.org/practice-resources/pep/prevention-infection
of disposal equipment when available (Kawamura, Ohmagari, Noda, Sugiyama, & Kurai, 2013; Montecalvo et al., 1999; Shaikh et al., 2002).

Environmental Interventions
Environmental interventions include disinfection and sterilization of surfaces and equipment, air filtration, positive air pressure rooms, hand hygiene, and barrier protection from body fluids. The IDSA states that environmental factors are effective in preventing infections in the general oncology and HCT population (Freifeld et al., 2011). Hand hygiene is the most effective means of preventing infection in the hospital (Freifeld et al., 2011; Stoll, Silla, Cola, Splitt, & Moreira, 2013). Patients undergoing HCT should have private rooms; allogeneic HCT recipients should have rooms with more than 12 air exchanges, high efficiency particulate absorption filtration, and positive pressure (Freifeld et al., 2011; Stoll et al., 2013). Plants and dried or fresh flowers are not allowed in rooms of hospitalized neutropenic patients (Freifeld et al., 2011). There is no evidence that protective gear (gowns, gloves, and masks) are effective in preventing infection when caring for neutropenic patients (Freifeld et al., 2011).

Diet
Studies have not shown a decrease in the incidence of infection with use of the low-microbial diet, which prohibits fresh fruits and vegetables and unprocessed food (Sonbol, Firwana, Diab, Zarzour, & Witzig, 2015; van Dalen et al., 2012, 2016). Standard food safety practices that emphasize safe handling and washing or thoroughly cooking food were found to be just as safe and produced no increase in infection rates or incidence of neutropenic fever (Gardner et al., 2008; Moody, Finlay, Mancuso, & Charlson, 2006).

Implications for Practice
Nurses caring for patients with cancer-related neutropenic sepsis must be aware that the mortality rate ranges from 2%-21% (Phillips et al., 2012). Evidence-based practice for prevention and management of infection, FN leading to infection, and FN complications are available and should be implemented in all settings where systemic therapy is administered (see Figures 3 and 4). Organizational support to develop documentation and tracking in the patient’s record will encourage timely, accurate, and consistent identification of risks, interventions, and related outcomes. Policies and practices that do not demonstrate benefit need to formally be discontinued so that time and resources can be allocated to activities and interventions proven to be beneficial in prevention of infection in the cancer treatment setting. Additional information for practice, which includes evidence summaries for the articles included in this review and other clinical tools and references, is available at www.ons.org/practice-resources/pep/prevention-infection.

Implications for Research
Hospitalized patients with cancer who have neutropenic complications experience higher all-cause mortality rates and higher inpatient hospitalization costs. The current evidence, although robust in volume, lacks the ability to replicate findings, and many of these studies are nonrandomized, single-institution studies with small sample sizes. Specific examples include studies for fungal prophylaxis that are limited by design, sample size, and low level of evidence, with the strongest level of evidence in HCT. In conjunction with the ONS (2015) strategic plan, oncology nurses at all levels continue to advance the quality of cancer care and patient/staff safety. These findings should inspire new questions leading to additional research, which may have a broader impact in the prevention of infection.

Conclusion
Prevention of infection is essential for successful cancer treatment and reduction of morbidity, mortality, and cost of oncology care. Current practice guidelines for prevention of infection in patients with cancer recommend risk assessments for early identification of infection, cancer-related FN, and FN complications for timely implementation of targeted, evidence-based interventions. ONS PEP for infection is a comprehensive synthesis of currently published nursing and medical research literature providing up to date best evidence resources to guide best oncology nursing practices for preventing infection in patients with cancer.
factor to reduce the incidence of chemotherapy-induced febrile neutropenia in adult patients with lymphoproliferative disorders and solid tumours. European Journal of Cancer, 47, 8–32. https://doi.org/10.1016/j.ejca.2010.10.013


