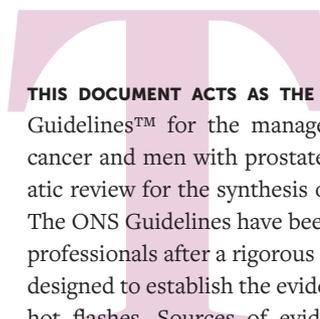


Hot Flashes

Clinical summary of the ONS Guidelines™ for cancer treatment–related hot flashes in women with breast cancer and men with prostate cancer

Marcelle Kaplan, MS, RN, CNS, Suzanne M. Mahon, DNSc, RN, AOCN®, AGN-BC, Barbara G. Lubejko, MS, RN, and Pamela K. Ginex, EdD, RN, OCN®

Cancer-related hot flashes are often a lasting and distressing side effect of hormone-blocking therapies that are most often experienced by women with breast cancer and men with prostate cancer treated with these therapies. Hot flashes have been defined as a sensation of heat that may be accompanied by facial flushing, perspiration, chills, heart palpitations, night sweats, and feelings of anxiety. The frequency and intensity of hot flashes can cause fatigue and sleep disturbances that diminish quality of life and reduce adherence with prescribed therapies that block estrogens or androgens. Hot flashes are reported to be significantly more frequent and severe in women treated for breast cancer than in women undergoing natural menopause. They also commonly occur in men treated for prostate cancer with surgical or chemical castration to block the synthesis of androgens that can fuel cancer growth.



THIS DOCUMENT ACTS AS THE CLINICAL SUMMARY component of the ONS Guidelines™ for the management of hot flashes in women with breast cancer and men with prostate cancer (Kaplan et al., 2020) and the systematic review for the synthesis of evidence on the topic (Hutton et al., 2020). The ONS Guidelines have been developed by a panel of oncology healthcare professionals after a rigorous systematic review of randomized clinical trials designed to establish the evidence-based efficacy of interventions to manage hot flashes. Sources of evidence have been divided into pharmacologic and nonpharmacologic interventions. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology approach was used to assess the certainty of the evidence and make the hot flash management recommendations that are presented in this clinical summary (Guyatt et al., 2011). The guidelines article can be found at <https://bit.ly/2BqRgzd> and the systematic review can be found at <https://bit.ly/2XAZVrN>.

Guideline Questions and Target Audience

What are the nonhormonal pharmacologic, physical/behavioral, and natural health product interventions that minimize the frequency and severity of hot flashes and their negative impact on quality of life in patients with breast or prostate cancer? The target audience for this guideline are clinicians who care for patients treated for breast or prostate cancer, policymakers, and patients and their caregivers.

How the Guideline Was Developed

This guideline was developed by an interprofessional panel of healthcare professionals, methods experts, and a patient representative. The panel prioritized clinical questions related to the management of cancer treatment–related hot flashes and patient outcomes identified as critical for decision making. A systematic review and network meta-analysis of the literature was conducted to inform the clinical questions (Hutton et al., 2020).

Why the Guideline Matters

Hot flashes are a distressing and often prolonged side effect experienced by women and men with cancer who are treated with hormone-blocking therapies or surgeries that abruptly suppress production of estrogen or testosterone. Hot flashes are reported to be much more frequent and severe in women treated for breast cancer than in women undergoing natural menopause (Carpenter, 2005; Kadakia et al., 2012). An estimated 51% to 81% of women treated for breast

KEYWORDS

hot flashes; breast cancer; prostate cancer; symptom management; guidelines

DIGITAL OBJECT IDENTIFIER

10.1188/20.CJON.E43-E46

cancer will experience hot flashes (Fisher et al., 2013). Almost 80% of men with prostate cancer treated with androgen-deprivation therapies (i.e., drugs or orchiectomy) will experience hot flashes, which can persist for years (Qan'ir et al., 2019).

Hormone therapies, such as estrogen replacement, although reported to be effective in managing hot flashes in postmenopausal women, are generally contraindicated in patients with a history of hormone-dependent cancer (Fisher et al., 2013). If hot flashes become too severe, there is a risk the patient will discontinue cancer treatment and, therefore, increase the risk of recurrence (Kadokia et al., 2012).

Clinical Practice Recommendations

Assessment of Hot Flashes

Hot flashes are a subjective experience and, as such, clinicians need to identify and educate patients who are at risk. Patients should be encouraged to bring concerns about hot flashes to their healthcare team and be informed that evidence-based interventions are available for treatment. These interventions can start when symptoms first appear. Hot flashes can diminish quality of life and even adherence to cancer therapies; therefore, early intervention is important to help mitigate the detrimental effect of hot flashes (Kadokia et al., 2012).

For patients with breast cancer or prostate cancer who are at high risk, clinicians should routinely assess for the presence of hot flashes and assess their severity and frequency. Self-reported hot flash diaries are an easy and informative option in clinical practice for patient report of this experience (Hanisch et al., 2009; Loprinzi & Barton, 2009). Patients can use the diary to note the frequency, severity, and intensity of daily hot flashes and how they interfere with daily activities, and are a good tool to inform discussions with their healthcare team.

Interventions for Hot Flashes

PHARMACOLOGIC INTERVENTIONS: Medications, particularly antidepressants, should be offered for treatment for patients experiencing hot flashes. Although research suggests a potential for benefit, these medications do have side effects. Most antidepressants studied have reasonable side effect profiles; however, medication interactions and patient history are important components of a shared decision-making process to identify the appropriate treatment. Antidepressants may not work immediately, and patients may need to take them for six to eight weeks to see a benefit.

The ONS Guidelines panel identified several antidepressants that may provide relief compared with no treatment. For women, the panel suggests venlafaxine, paroxetine, clonidine, sertraline, fluoxetine, escitalopram, or duloxetine. Among these antidepressants, the panel suggested women use venlafaxine or paroxetine as first-line therapy, followed by clonidine, and then sertraline, fluoxetine, escitalopram, or duloxetine for the management of symptoms. For men, the panel suggests paroxetine, clonidine,

“Patients should be encouraged to bring concerns about hot flashes to their healthcare team.”

sertraline, fluoxetine, escitalopram, or duloxetine. Among these agents, the panel suggests men use paroxetine or clonidine as first-line therapy followed by sertraline, fluoxetine, escitalopram, or duloxetine for the management of symptoms. Although antidepressants can be effective, paroxetine and some other selective serotonin reuptake inhibitors that inhibit CYP2D6 are contraindicated in women and men who are treated with tamoxifen (Kaplan et al., 2020) (see Table 1).

NONPHARMACOLOGIC INTERVENTIONS: There is growing evidence that physical activity interventions to manage hot flashes can be beneficial. The ONS Guidelines panel suggests engaging in physical activities, such as exercise programs and yoga, over no treatment for the management of symptoms (Kaplan et al., 2020).

Clinical Practice Interventions Not Recommended

Gabapentinoids are sometimes recommended as treatment for hot flashes. The studies reviewed for this guideline, as well as more recent reports, identify serious side effects of gabapentinoids. These side effects include breathing difficulties in patients taking other medications that depress the central nervous system, such as opioid pain medicines, or in patients with comorbidities, such as chronic obstructive pulmonary disease, as well as in older adults (U.S. Food and Drug Administration, 2019). Because of the potential side effects and these reports, the ONS Guidelines panel suggests against treatment with gabapentinoids for the management of hot flashes (Kaplan et al., 2020).

The evidence on dietary supplements is limited with a lack of known benefit and unknown or potential harms. Because of the limited evidence, the ONS Guidelines panel suggests against the use of herbal or dietary supplements (soy, black cohosh, St John's wort, melatonin, vitamin E) for the management of hot flashes (Kaplan et al., 2020).

Interventions Without Sufficient Evidence

Several interventions for the management of hot flashes in patients with cancer require additional evidence. Venlafaxine

TABLE 1.
SUMMARY OF RECOMMENDATIONS: ONS GUIDELINES™ FOR HOT FLASHES IN PATIENTS WITH CANCER

| RECOMMENDATION | STRENGTH OF RECOMMENDATION | CERTAINTY OF EVIDENCE |
|---|----------------------------------|-----------------------|
| Pharmacologic recommendations for women with breast cancer | | |
| Recommendation 1: For women with breast cancer who are experiencing drug- or surgery-induced hot flashes, the ONS Guidelines panel suggests using venlafaxine, paroxetine, or clonidine rather than no treatment for the management of symptoms or (Recommendation 2) the panel suggests using sertraline, fluoxetine, escitalopram, or duloxetine rather than no treatment for the management of symptoms. ^a | Conditional | Low/very low |
| Recommendation 3: Among these pharmaceuticals, the panel suggests using venlafaxine, paroxetine, or clonidine rather than sertraline, fluoxetine, escitalopram, or duloxetine for the management of symptoms. ^a | Conditional | Very low |
| Recommendation 4: Among venlafaxine, paroxetine, or clonidine, the panel suggests using venlafaxine or paroxetine rather than clonidine for the management of symptoms. ^a | Conditional | Low |
| Remarks: Patients who have not responded to treatment with venlafaxine or paroxetine may wish to try clonidine to manage hot flash symptoms. Patients who have not responded to venlafaxine, paroxetine, or clonidine may wish to try these antidepressants: sertraline, fluoxetine, escitalopram, or duloxetine. ^a | | |
| Pharmacologic recommendations for men with prostate cancer | | |
| Recommendation 5: For men with prostate cancer who are experiencing drug- or surgery-induced hot flashes, the panel suggests paroxetine or clonidine rather than no treatment for the management of symptoms or (Recommendation 6) the panel suggests sertraline, fluoxetine, escitalopram, or duloxetine rather than no treatment for the management of symptoms. | Conditional | Low/very low |
| Recommendation 7: Among these pharmaceuticals, the panel suggests paroxetine or clonidine rather than sertraline, fluoxetine, escitalopram, or duloxetine for the management of symptoms. | Conditional | Very low |
| Remarks: Patients who have not responded to treatment with paroxetine or clonidine may wish to try the following antidepressants: sertraline, fluoxetine, escitalopram, or duloxetine. | | |
| Recommendation 8: For men with cancer who are experiencing drug- or surgery-induced hot flashes, the panel recommends venlafaxine for the management of symptoms only in the context of a clinical trial. | No recommendation; knowledge gap | – |
| Pharmacologic recommendations for women with breast cancer or men with prostate cancer | | |
| Recommendation 9: For patients with cancer who are experiencing drug- or surgery-induced hot flashes, the panel suggests against gabapentin or pregabalin (gabapentinoids) for the management of symptoms. | Conditional | Very low |
| Nonpharmacologic recommendations for women with breast cancer or men with prostate cancer | | |
| Recommendation 10: For patients with cancer who are experiencing drug- or surgery-induced hot flashes, the panel suggests against herbal or dietary supplements (soy, black cohosh, St. John's wort, melatonin, vitamin E) for the management of symptoms. | Conditional | Very low |
| Recommendation 11: Among patients with cancer experiencing drug- or surgery-induced hot flashes, the panel recommends hypnosis or relaxation therapy only in the context of a clinical trial. | No recommendation; knowledge gap | – |
| Recommendation 12: Among patients with cancer experiencing drug- or surgery-induced hot flashes, the panel recommends cognitive behavioral therapy only in the context of a clinical trial. | No recommendation; knowledge gap | – |
| Recommendation 13: Among patients with cancer experiencing drug- and surgery-induced hot flashes, the panel suggests physical activity interventions (exercise, yoga) rather than no treatment for the management of symptoms. | Conditional | Low |
| Recommendation 14: Among patients with cancer experiencing drug- or surgery-induced hot flashes, the panel recommends acupuncture and electroacupuncture only in the context of a clinical trial. | No recommendation; knowledge gap | – |
| <p>^aParoxetine and fluoxetine are strong CYP2D6 inhibitors and may significantly interfere with tamoxifen metabolism and, therefore, are contraindicated in women taking tamoxifen. ONS—Oncology Nursing Society</p> <p>Note. From "ONS Guidelines for Cancer Treatment-Related Hot Flashes in Women With Breast Cancer and Men With Prostate Cancer," by M. Kaplan, P. Ginex, L.B. Michaud, P. Fernandez-Ortega, D. Grimmer, J. Bay Leibel, . . . R.L. Morgan, 2020, <i>Oncology Nursing Forum</i>, 47(4), pp. 378–379. Copyright 2020 by Oncology Nursing Society. Reprinted with permission.</p> | | |

has been studied in women with breast cancer, but research is limited for men with prostate cancer. Several nonpharmacologic interventions, such as hypnosis or relaxation therapy, cognitive behavioral therapy, and acupuncture or electroacupuncture have been used for hot flashes, but additional research is needed to learn more about the benefits, clinical feasibility, and harms of these interventions. The ONS Guidelines panel recommends these interventions only in the context of a clinical trial so that additional research can be gathered to inform future guidelines (Kaplan et al., 2020).

Implications for Nursing

Hot flashes can significantly affect quality of life for patients on hormone-blocking cancer treatment, and healthcare professionals should assess for the presence and impact of hot flashes for patients at risk. Nurses and other healthcare professionals should use evidence-based measures to decrease the severity and number of hot flashes with the goal to improve quality of life and patient outcomes.

Conclusion

This guideline addressed the following overarching question: “What are the nonhormonal pharmacologic, physical/behavioral, and natural health product interventions that minimize the frequency and severity of hot flashes in patients with breast or prostate cancer?” The guideline was developed using rigorous methodology to assess the certainty and quality of the evidence for hot flash intervention. Hot flashes are a frequent and distressing side effect for patients, and clinicians should assess patients at risk and discuss treatment options. Evidence-based interventions are available, and patients who are experiencing hot flashes have options to consider.

Marcelle Kaplan, MS, RN, CNS, is an oncology nursing consultant in Merrick, NY; **Suzanne M. Mahon, DNSc, RN, AOCN[®], AGN-BC**, is a professor in the Division of Hematology/Oncology and an oncology professor in the School of Nursing at Saint Louis University in Missouri; **Barbara G. Lubejko, MS, RN**, is a nursing education and medical writing consultant in Ocean City, MD; and **Pamela K. Ginex, EdD, RN, OCN[®]**, is the senior manager of evidence-based practice and inquiry at the Oncology Nursing Society in Pittsburgh, PA. Ginex can be reached at pginex@ons.org, with copy to CJONEditor@ons.org. (Submitted May 2020. Accepted May 11, 2020.)

The authors gratefully acknowledge the members of the ONS Guidelines panel as well as Brian Hutton, MSc, PhD, and his team at the Ottawa Hospital Research Institute for their collaboration and assistance in using the network meta-analysis data for the guideline.

IMPLICATIONS FOR PRACTICE

- Assess patients with breast or prostate cancer who are at risk for hot flashes. This assessment should include history of the presence, severity, and frequency of hot flashes.
- Discuss pharmacologic and nonpharmacologic interventions with patients who are reporting bothersome hot flashes and identify which intervention would be most appropriate for each patient.
- Understand that some pharmacologic interventions, such as use of the antidepressants paroxetine and fluoxetine, are contraindicated in patients taking tamoxifen. These drugs should be avoided because they interfere with the metabolism of tamoxifen. Venlafaxine would be a better option for these patients.

Development of the guideline on which this clinical summary was based was wholly funded by the Oncology Nursing Society, a nonprofit organization that represents oncology nurses. No honoraria were provided.

REFERENCES

- Carpenter, J.S. (2005). State of the science: Hot flashes and cancer, part 1: Definition, scope, impact, physiology, and measurement. *Oncology Nursing Forum*, *32*(5), 959–968. <https://doi.org/10.1188/05.ONF.959-968>
- Fisher, W.I., Johnson, A.K., Elkins, G.R., Otte, J.L., Burns, D.S., Yu, M., & Carpenter, J.S. (2013). Risk factors, pathophysiology, and treatment of hot flashes in cancer. *CA: A Cancer Journal for Clinicians*, *63*(3), 167–192. <https://doi.org/10.3322/caac.21171>
- Guyatt, G.H., Oxman, A.D., Akl, E.A., Kunz, R., Vist, G., Brozek, J., . . . deBeer, H. (2011). GRADE guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables. *Journal of Clinical Epidemiology*, *64*(4), 383–394. <https://doi.org/10.1016/j.jclinepi.2010.04.026>
- Hanisch, L.J., Palmer, S.C., Marcus, S.C., Hantsoo, L., Vaughn, D.J., & Coyne, J.C. (2009). Comparison of objective and patient-reported hot flash measures in men with prostate cancer. *Journal of Supportive Oncology*, *7*(4), 131–135.
- Hutton, B., Hersi, M., Cheng, W., Pratt, M., Barbeau, P., Mazzarello, S., . . . Clemons, M. (2020). Comparing interventions for management of hot flashes in patients with breast and prostate cancer: A systematic review with meta-analyses. *Oncology Nursing Forum*, *47*(4), E86–E106. <https://doi.org/10.1188/20.ONF.E86-E106>
- Kadakia, K.C., Loprinzi, C.L., & Barton, D.L. (2012). Hot flashes: The ongoing search for effective interventions. *Menopause*, *19*(7), 719–721. <https://doi.org/10.1097/gme.0b013e3182578d31>
- Kaplan, M., Ginex, P., Michaud, L.B., Fernanedz-Ortega, P., Grimmer, D., Liebelt, J.B., . . . Morgan, R.L. (2020). ONS Guidelines™ for cancer treatment-related hot flashes in women with breast cancer and men with prostate cancer. *Oncology Nursing Forum*, *47*(4), 374–379. <https://doi.org/10.1188/20.ONF.374-379>
- Loprinzi, C.L., & Barton, D.L. (2009). Gadgets for measuring hot flashes: Have they become the gold standard? *Journal of Supportive Oncology*, *7*(4), 136–137.
- Qan'ir, Y., DeDeaux, D., Godley, P.A., Mayer, D.K., & Song, L. (2019). Management of androgen deprivation therapy-associated hot flashes in men with prostate cancer. *Oncology Nursing Forum*, *46*(4), E107–E118. <https://doi.org/10.1188/19.ONF.E107-E118>
- U.S. Food and Drug Administration. (2019, December 19). *FDA warns about serious breathing problems with seizure and nerve pain medicines gabapentin (Neurontin, Gralise, Horizant) and pregabalin (Lyrica, Lyrica CR)*. <https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-about-serious-breathing-problems-seizure-and-nerve-pain-medicines-gabapentin-neurontin>