

# EPEEC-O

Education in Palliative and End-of-life Care - Oncology

## **Participant's Handbook**

Module 3a:

**Symptoms -**

**General**

**Introduction**

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**EPEC-O: Education in Palliative and End-of-life Care for Oncology.**  
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**ISBN: 0-9714180-9-8**

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The EPEC Project™ was created with the support of the American Medical Association and the Robert Wood Johnson Foundation. The EPEC-O curriculum is produced by The EPEC Project™ with major funding provided by the National Cancer Institute, with supplemental funding provided by the Lance Armstrong Foundation. The American Society of Clinical Oncology partners with the EPEC-O Project in dissemination of the EPEC-O Curriculum. Acknowledgment and appreciation are extended to Northwestern University's Feinberg School of Medicine, which houses The EPEC Project.

Special thanks to the EPEC-O Team, the EPEC-O Expert Panel, and all other contributors.

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## Abstract

Many symptoms and syndromes are commonly encountered in patients with cancer. This module first presents general approaches to symptom management. Then, the management of the specific symptoms and syndromes are discussed, including: anorexia/cachexia, anxiety, constipation, depression, diarrhea, fatigue, insomnia, menopausal symptoms and sexual health, mucositis, nausea and vomiting, and skin problems.

Any symptom can both be debilitating and prevent the patient and family from achieving goals that are important to them. As with other aspects of medicine, tailored management is based on the underlying etiology and pathophysiology. When several symptoms occur together, they can be interrelated and management may be complex.

## Key words

Anorexia, asthenia, cachexia, constipation, diarrhea, fatigue, loss of appetite, nausea, vomiting, weight loss, mucositis, insomnia, hot flashes, depression, anxiety, skin, ulcers, dyspnea, delirium, bowel obstruction, malignant pleural effusions, ascites, and sedation for refractory symptoms, terminal sedation, multisymptom management, interdisciplinary team.

## Objectives

After studying this module, for each symptom and syndrome, oncologists and other members of the cancer care team will be able to:

- Discuss general assessment and management guidelines.
- Describe the possible causes and underlying pathophysiology.
- Conduct a careful assessment.
- Initiate an appropriate management strategy, including rapid and breakthrough dosing.
- Describe principles of multi-symptom management.
- Understand principles of double effect.

## Clinical case on trigger tape

This video case vignette can be used to trigger discussion of general approaches to symptom assessment and the management of dyspnea or nausea/vomiting.

M.S. is a 67-year-old businesswoman who notes exertional dyspnea that has gradually worsened over the past 3 years. She has inoperable stage IIIb non-small cell lung cancer and pulmonary fibrosis. She also has an 8 cm thoracic aortic aneurysm that is inoperable. When she is short of breath, she also notes feeling lightheaded and dizzy. She uses

oxygen at 2 liters per nasal canula that is delivered both by portable tanks and by a tank of liquid oxygen at home. She notes her breathing is better when she uses the big tank at home. She also notes chest pain under her left breast radiating to her left side and occasionally her left shoulder that is relieved with sublingual nitroglycerin. She also notes chronic nausea that is relieved by eating soda crackers. She also says she is anxious--she feels like she's a walking time bomb—ready to explode.

## Introduction

Most patients suffer from pain and number of other common symptoms. This module discusses many of the symptoms that are frequently seen in cancer care, including:

**Table 1: Common symptoms & syndromes in EPEC-O**

Anorexia/cachexia	Dyspnea
Anxiety	Fatigue
Ascites	Insomnia
Bowel obstruction	Malignant pleural effusions
Constipation	Menopausal symptoms
Delirium	Mucositis
Depression	Nausea/vomiting
Diarrhea	Skin problems

Several of the other EPEC-O modules present related topics. EPEC-O Module 1: Comprehensive Assessment discusses approaches to a comprehensive patient assessment. Pain is addressed in EPEC-O Module 2: Cancer Pain Management, and symptom management issues in the last hours of life, including terminal delirium and rattle, are discussed in EPEC-O Module 6: Last Hours of Living.

Some symptoms, such as fatigue, are more prevalent than pain. Others, such as dyspnea, can be more distressing to patients and families than pain. If unrelieved, they preclude any possibility of completing cancer treatment, or relieving psychological, social, and spiritual issues that are causing suffering, or improving quality of the patient's and family's life.

Symptoms are more than clues that can lead to diagnoses. It would be a mistake for oncologists to assume that symptoms all improve with anti-cancer treatment. While it is common for oncologists to direct their therapeutic efforts at the cancer, they will also want to understand the possible causes and pathophysiology associated with each symptom, and therapeutic interventions with the greatest potential for benefit and the least risk of causing harm or burden to the patient and family.

Symptoms frequently interfere with the patient's and family's capacity to do the things they like to do. They can impair the oncologist's ability to give anti-cancer therapy, particularly when the symptoms are the result of the anti-cancer treatment itself. If left unmanaged, they may lead to changes that shorten survival.

Conversely, if symptoms are well-managed and the patient can eat well, sleep well, maintain function and has minimal stress, s/he will be more likely to sustain full anti-cancer therapy and live a longer and more fulfilling life.

## General management guidelines

The general approach to managing a symptom is similar to the standard approach used to manage cancer:

- Prevention and early detection will not only alleviate suffering faster and more effectively, they may also prevent future complications that will be more challenging to manage.
- Therapies are chosen that have the greatest potential for benefit and the least risk of causing harm, eg, adverse events, and burden to the patient and family (following the ethical principles of beneficence, ie, the provision of benefits and the balancing of harms and benefits for the purpose of doing the most good, and nonmaleficence, ie, the avoidance of doing harm).
- Treat the cause and the experience. Use pharmacological, surgical, radiation, chemotherapeutic agents as appropriate. Consider clinical trials, including phase I trials as appropriate, keeping in mind that full palliative care during the trial is necessary and rarely restricted.
- For multiple symptoms, rationalize the therapeutic approach to minimize the number and potential interferences among interventions.

## Understand the underlying cause and pathophysiology

As symptoms are often interrelated with concurrent medical problems, management can be challenging. As with any illness, it is not sufficient to have a simplistic approach to symptom management, as causes and appropriate therapies can vary widely. Before embarking on the management of a symptom, have a conceptual framework of the possible causes and associated pathophysiology to guide assessment and management. Frameworks are presented in each of the symptom management modules that follow.

Besides the physical manifestations of a symptom, always look for the influence of psychological, social, spiritual, end of life, and loss issues. Dame Cicely Saunders was the first to understand these interrelationships with her description of 'total pain' in the 1960's.<sup>1</sup> Spiritual pain may be expressed as physical pain. Dyspnea causes anxiety. Uncontrolled symptoms interrupt psychosocial relations. A comprehensive assessment

(see EPEC-O Module 1: Comprehensive Assessment) will be helpful in discerning the underlying cause of individual symptoms.

## Assess carefully

For each symptom, conduct a thorough assessment including a history/functional inquiry, physical examination, and laboratory and/or radiologic investigations appropriate for the patient’s situation. Use this information to gain the best possible understanding of the cause and underlying pathophysiology for each symptom, and guide management.

The occurrence of a number of symptoms is highly predictable, eg, nausea, constipation, anxiety with pain therapy. Assess for these symptoms routinely during your functional inquiry. Include strategies to prevent/manage them in your treatment plan, eg, prescribe antiemetics with chemotherapy and a bowel regimen to preempt opioid-induced constipation, counsel the patient and family as soon as they present with a serious new illness to preempt adjustment disorders.

For each symptom, collect basic data about the onset, location, description of the experience, temporal profile (change over time), severity, the effect of medications and the presence of any adverse effects (see Table 1). Based on patient preferences, use any one of the assessment scales in Figure 2 to assess severity. Look for the importance of psychological, social, spiritual end-of-life and loss issues

**Table 1: Basic symptom assessment**

1. Onset
2. Location
3. Description / quality
4. Temporal profile
5. Severity
6. Effect of medications
7. Adverse effects

on the symptom. To this end, develop a consistent channel for family communication. Having diverse perspectives helps to clarify what is happening and minimizes the risk of miscommunication and conflict.

Carefully collected data will facilitate clear communication between team members and guide

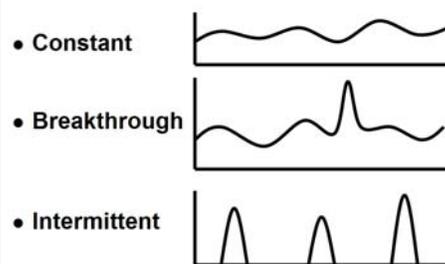
management choices. Comparison of assessments from one day to the next will establish the effectiveness of therapeutic interventions.

## Manage quickly

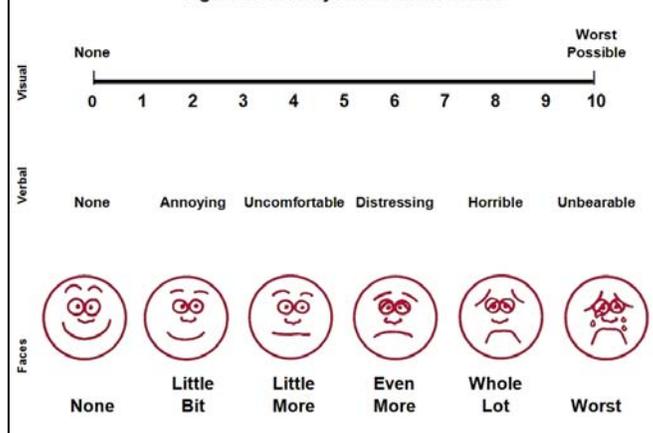
The ideal plan of care includes therapies to both:

- Treat the cause of the symptom.

**Figure 1: Common temporal profiles**



**Figure 2: Severity Assessment Scales**



- Manage the experience.

Many journal articles and textbooks have been written on the management of the underlying causes, and this module focuses primarily on managing the experience caused by the symptom.

When symptoms are severe or the patient is weak, oncologists will not be able to wait for the results of investigations to initiate therapy. Initial therapeutic efforts based on history, examination, and inference about the underlying pathophysiology may produce symptom relief and provide additional information as to the cause and pathophysiology.

When the patient's goals for care preclude disease management, symptom relief to manage the experience may become the total focus of care.

Always consider both pharmacological and non-pharmacological therapeutic interventions to manage symptoms, including counseling and complementary therapies.

To ensure consistent care planning and delivery, work closely with members of the interdisciplinary cancer care team. As changes in the patient's condition can occur rapidly, be prepared to respond quickly.

Choose medications appropriate for the underlying cause and pathophysiology, and the severity of the symptom. Plan dosing strategies based on the temporal profile of the symptom, the pharmacokinetics of the medication and the patient's lifestyle. Most of the medications used in palliative care follow simple first-order kinetics. Fortunately, most of the clinical responses to these medications correlate closely with their plasma concentration.

## **Continuous dosing**

For a symptom that is constantly present 'around-the-clock', provide the medication routinely once every half-life ( $t_{1/2}$ ). When the medication follows first-order kinetics, steady state will be reached within 5 half-lives. Try not to adjust the routine dose before steady state has been reached. Premature adjustments increase the risk of unwanted adverse effects. See the Medication Tables in EPEC-O for specific  $t_{1/2}$ ,  $t_{C_{max}}$ , and dosing data.

## **Breakthrough / intermittent dosing**

For acute breakthrough or intermittent exacerbations of a symptom, extra or breakthrough doses of medication can be offered once every 'time to maximum concentration' (time<sub>C<sub>max</sub></sub>). Choose a medication whose absorption-excretion profile comes as close as possible to the temporal profile of the acute exacerbation of the symptom. As an example, the use of morphine ( $t_{1/2} = 4$  hours) to manage movement-related breakthrough pain that lasts 5-10 minutes will inevitably lead to unwanted drowsiness and other adverse effects.

Many cancer patients experience multiple concurrent symptoms. Their management is the daily challenge of palliative care. Occasionally, a patient may need to decide which

symptoms need to be managed more than others. Optimal use of non-invasive, non-pharmacological approaches, eg, use of enteral/mucosal routes of administration before parenteral, use of sleep hygiene before pharmacological therapy, can be helpful.

A well-rationalized medication list minimizes the risk of drug interaction that comes with polypharmacy. Especially in patients with late stage disease, declining renal or hepatic function, reduced fat and general frailty, be aware of altered pharmacokinetics, particularly when there is a risk that clearance will be impaired. Whenever possible, choose one medication to treat more than one symptom, eg, use steroids to reduce fatigue and improve the pain of bony metastases. Be aware when treatment of one symptom later conflicts with an emerging issue, eg, non-steroidal anti-inflammatory agents may need to be discontinued if a wound fails to heal. Specific instances of multi-symptom management can be found throughout the symptom management modules.

## **Rationalize management of multiple symptoms**

Since many cancer patients have many symptoms, management of multiple symptoms is the daily challenge of palliative care. Occasionally, a patient may need to decide which symptom's management is the highest priority, but the goal is to be able to manage all symptoms.

Optimal use of non-invasive, non-pharmacological approaches, eg, use of enteral medication routes before parenteral, use of sleep hygiene before pharmacological therapy, can assist.

A well-rationalized medication list that avoids the hazards of polypharmacy is essential. Especially in patients with late stage disease, declining renal or hepatic function, reduced fat and general frailty, medication side-effects can be devastating in their own right. Be aware of medications that can accumulate.

Choose one agent to treat more than one symptom whenever possible, eg, use of steroids to improve reduce fatigue and the pain of bony metastases. Be aware when treatment of one symptom later conflicts with an emerging issue, eg, non-steroidal anti-inflammatory agents may need to be discontinued if diuresis for ascites has become a problem, or a patient on a serotonin antagonist who starts to need opioids may need an alternative as part of expectant or proactive management of constipation.

Specific instances of multi-symptom management can be found throughout the symptom management modules (EPEC-O Module 3: Symptoms).

## **Coordinate care**

### **Educate the patient, family, and caregivers**

Education and involvement of the patient, family, and all caregivers as partners is key to successful symptom management. After their initial education and training in specific

caregiving skills, they will likely need considerable reinforcement and support to optimize the plan of care.

Encourage the patient and family to keep a diary when symptoms are out of control or adverse effects occur. Each time the patient takes a dose of medication, record the date and time, present severity of the symptom, medication and dose used, and any adverse effects at that time.

**Table 2: Symptom diary**

Date, time	Severity	Medication used	Adverse effects

### **Include the interdisciplinary team**

Symptoms are experienced in multiple domains and the busy oncologist can rarely discharge all the duties of comprehensive care without the assistance of an interdisciplinary team. The oncologist will need to ensure that the nurse, social work, pharmacy, and pastoral members of the team are all coordinating in the implementation of a single care plan to attend to the cancer patient's many needs. Regular team meetings, attention to communication and coordination are essential in quality comprehensive cancer care.

### **Palliative care consultations**

When symptom management becomes complex or they do not resolve quickly, consult with a palliative medicine expert to help optimize therapies and minimize the risk of adverse events and drug interactions.

### **Reassess periodically**

As etiologies and pathophysiology may change, frequent reassessment and review of the goals of care, treatment priorities, and plan of care is critical, particularly when symptoms recur or worsen.

## **Intended vs. unintended consequences**

Many physicians believe that medications used to manage symptoms have an unusually or unacceptably high risk of an adverse event that may shorten a patient's life, particularly when he or she is frail or close to the end of his or her life. Instead of fully

understanding and discussing the potential benefits and risks of these therapies with their patients, taking into account their goals for care, this fear of an adverse unintended consequence often leads clinicians to withhold treatment or dose inadequately, thus leaving their patients suffering unnecessarily.

When offering a therapy, the intent in offering a treatment that greatly determines whether it is ethical medical practice:

- If the intent in offering a treatment is desirable or helpful to the patient and the primary outcome is good (such as cure or relief of suffering), but there is a potential, adverse, secondary effect (such as death), then the treatment is probably still ethical if there was proper informed consent.
- If the intent is not desirable or will harm the patient and the primary outcome is bad, the treatment is probably unethical.

Concerns about intended vs. unintended consequences are most commonly invoked around such issues as the treatment of pain or dyspnea with opioids. However, all medical treatments have both intended effects and the risk of unintended, potentially adverse, secondary consequences. Some examples are listed in table 3:

**Table 3: Intended vs. unintended consequences**

Therapy	Intended, primary effect	Potential adverse, secondary consequences
TPN for short gut syndrome	Improved nutritional status	Sepsis, death
Chemotherapy	Cure or reduce the burden of cancer	Immune suppression, cytopenias, death
Amiodarone	Prevent arrhythmia	Promote arrhythmia, death
Epidural administration of analgesia	Reduce pain	Sepsis, death
Stopping all lab tests	Reduce burden of investigation for patient	Electrolyte imbalance, death
Operation to repair broken hip	Reduce pain, improve function	Cardiac arrest, death during surgery

## Principle of double effect

The principle of double effect refers to an ethical construct when a person takes an action with an expected good outcome but with an unavoidable, known bad effect as well (in 100% of patients). The primary intended effect can sometimes justify the action. When a physician uses a treatment for an ethical, intended effect where the potential outcome is good, eg, relief of a symptom, knowing that there may also be a dire, undesired,

secondary effect such as death, this principle of double effect is commonly cited. In symptom control, however, it rarely applies. The secondary adverse consequence of death is not likely to occur.

## **Concerns about symptom management**

Concerns that the principle of double effect may be an issue when managing symptoms are raised by the fact that, like other medical treatments, there is a risk that treatments to control symptoms could produce adverse consequences including death, either when improperly used or, very rarely, when properly used. Also, in suffering states of life-threatening illness, death may seem appealing and what is ordinarily intuitive may become complex. For many interventions, such as chemotherapy, total parenteral nutrition for short gut syndrome, surgery, and noninterventions such as stopping all laboratory tests or avoiding surgery, we make decisions knowing there is a risk of adverse events, in particular death. As long as (a) the intent is to relieve suffering and not hasten death, (b) death is a possible and not inevitable outcome of the interventions, and (c) there is fully informed consent, the action need not be ethically suspect.

In contrast, if symptom control involves treatments that are intended to cause death as the means to relieve suffering, then there is ethical concern. If the patient seeks hastened death by physician-assisted suicide or euthanasia, the clinical and ethical issues are different. Some of these issues are addressed in EPEC-O Module 14: Physician-Assisted Suicide.

Fortunately, these difficult circumstances need not occur. Adequate symptom management can be achieved without causing death. If the reason for offering a medication such as an opioid is to relieve suffering, eg, pain, breathlessness, and accepted dosing guidelines are followed, the risk of a potentially dangerous adverse secondary effect is minimal. The risk of respiratory depression is vastly over estimated. Patients will become drowsy and confused and lose consciousness long before their respiratory rate is compromised.

Symptoms can be well controlled with the interventions outlined in this module and those in EPEC-O Module 2: Cancer Pain Management and EPEC-O Module 6: Last Hours of Living. None of these recommendations, properly used, will cause death. In this, they are like all other medical interventions; concerns about unintended consequences are no greater than normal and concerns about double effect rarely apply.

## **Terminal sedation**

Occasionally, refractory symptoms lead the patient, family, and professional team to conclude that the only option for securing comfort for the patient is sedation. If it is not possible to lighten the sedation without a return to unbearable suffering, this sedation can be terminal.

Terminal sedation has been somewhat controversial. Concerns have been raised, for instance, about the use of nutrition and hydration during sedation, and about whether the complexity of human intentions can allow for a clear enough moral boundary in the application of the principle of double effect. Feelings can run very high when terminal sedation is being considered. Technical expertise in the procedure is also necessary.

For all these reasons, although it is clearly identified as good practice in some well defined circumstances, terminal sedation should not be conducted without involvement of palliative care experts. Even in circumstances when access to a palliative care expert is difficult, every effort should be made to gain their involvement even if only by telephone.

## Summary

Symptom control requires the physician to combine scientific knowledge of pathophysiology, pharmacotherapeutics, and human behavior with communication skills and clinical judgment. Multiple symptoms are present for most cancer patients, making management particularly challenging. Careful attention to symptom control may lead to better tolerance of disease-modifying therapies, and may even help prolong life. It is challenging and rewarding to help patients feel better no matter what the status of the underlying cancer. Continued symptom control as patients approach the end of their lives will give them the opportunity to realize the personal goals for which they are striving and to die comfortably.

## Key take-home points for general management

1. Symptoms demand active management, along with cancer treatment, as part of comprehensive cancer care.
2. Initial therapeutic efforts based on a comprehensive assessment, and inference about the pathophysiology may provide both symptom relief and/or additional information as to the etiology and pathophysiology of the symptom.
3. Where possible and consistent with the goals of care, treat the underlying cause of each symptom, but do not delay efforts to manage the experience.
4. Manage quickly; use continuous and break-through dosing.
5. Rationalize the treatment plan to take the multiple symptoms and adverse effects of medications into account as well as the need for renal and hepatic dosing.
6. Rely on the interdisciplinary team for optimal patient experience.

## Pearls

1. Accept the patient's self-report of his or her experience.
2. Assess how much the patient (as opposed to family) is bothered by symptoms. Frequently the patient is comfortable, but the family is distressed.

3. When patients have multiple symptoms, ask which one is most important to improve—frequently it’s not the one you thought it would be.
4. When treating multiple symptoms, choose drugs that can manage more than one symptom, eg, opioids manage pain and breathlessness, metoclopramide for nausea also helps with constipation.
5. Non-pharmacologic techniques may also provide significant relief.
6. A symptom is easier and far less costly to prevent than treat.

## Pitfall

1. Don’t try to fix a symptom that isn’t bothering the patient.

## Resources

Doyle D(ed), Hanks G(ed), MacDonald N(ed.). *Oxford textbook of palliative medicine*. New York, NY: Oxford University Press; 1993. ISBN: 0192620282

*ASCO Curriculum on Symptom Management, Vol.1*. Dubuque, IA: Kendall/Hunt Publishing; 2001. ISBN 0-7872-8204-9

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## References

- <sup>1</sup> Clark D. 'Total pain', disciplinary power and the body in the work of Cicely Saunders, 1958-1967. *Soc Sci Med*. 1999 Sep;49(6):727-36. [PMID: 10459885](#). [Full Text](#).

A review of the evolution of Dame Cicely Saunders thinking about ‘Total pain.’