

B.C. INTER-PROFESSIONAL PALLIATIVE SYMPTOM MANAGEMENT GUIDELINES

SYMPTOMS TO EXPLORE



AUDIENCE

Inter-professional clinicians working with adults living with advanced life-limiting illnesses. Though these guidelines were created for adults, the symptoms may also be experienced by children. See additional resources within each guideline specific to pediatrics, illnesses such as cancer, and your organization/region.

CONTRIBUTING PARTNERS



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LETTER OF INTRODUCTION – DR. DORIS BARWICH

The BC Centre for Palliative Care is thrilled to have been able to support the development of these updated B.C. Inter-professional Palliative Symptom Management Guidelines for Inter-Disciplinary providers in BC. It has been an exciting project involving many expert clinicians as well as front-line providers to ensure a product that not only ensures best practices but is also accessible and user-friendly for health care providers throughout BC. Enabling quality of life for patients and families with serious illness is core to what we do. Enabling excellence in pain and symptom management 24/7 throughout BC will ensure quality of care and improve outcomes for patients and families.

A big thank you to all our partners who helped make it possible.



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BACKGROUND AND DEVELOPMENT OF THE B.C. PALLIATIVE SYMPTOM MANAGEMENT GUIDELINES

The Fraser Health Hospice Palliative Care Program's Symptom Management Guidelines (Fraser SMGs) were first introduced in Dec 2006. Since then, some have been updated and the 4th edition (2012) is currently available on the Fraser Health website¹. Island Health, Interior Health and Northern Health have adapted and adopted the Fraser Health SMGs as Best Practice Guidelines. Vancouver Coastal uses their Community Palliative Care Clinical Practice Guidelines,² while First Nations Health Authority utilized guidelines from their nearest regional health authority.

Educators and clinical leaders from the health authorities using the Fraser SMGs acknowledged a lack of sufficient resources to independently update them and expressed interest in a collaborative process. They offered in kind contribution by palliative educators and clinicians to further the provincial effort.

In addition to the request from regional health authorities, the BC Ministry of Health recognized the need for provincial guidelines for end of life care. The BC Center for Palliative Care (BC-CPC) was mandated by the Ministry to support the creation of new hospice spaces by:

- Promoting excellence in end of life care and innovation / best practices in end of life care;
- Implementing provincial end of life clinical guidelines, protocols and standards³.

In March of 2016, the project, "Palliative Symptom Management Guidelines; a resource for British Columbia" was approved by the sponsor, Dr. Doris Barwich (Executive Director, BC-CPC) with the goal of creating a provincial set of palliative symptom management best practice guidelines which were:

- Informed by evidence current to May 2016;
- Endorsed by each health authority in B.C.

The objectives of the project were to:

- Utilize an agreed-upon, documented methodology for evidence review;
- Provide a toolkit for future guideline revisions, informed by lessons learned during this project;
- Create an opportunity for provincial collaboration towards shared goals.

1 Fraser Health. "Hospice Palliative Care Symptom Guidelines". Accessed Feb 8, 2016. <http://www.fraserhealth.ca/health-professionals/professional-resources/hospice-palliative-care/>

2 Vancouver Coastal Health. "Community Palliative Care Clinical Practice Guidelines", 2007.

3 BC Center for Palliative Care Strategic Plan 2015

DEVELOPMENT PROCESS: PHASES 1 - 3

Phase 1 Stakeholder engagement and scoping of the project (March-June, 2016)

The primary goal of Phase 1 was the establishment of a provincial Steering Committee that would provide leadership and guidance throughout the project. The committee was comprised of representatives from six health authorities (Fraser, Providence, First Nations, Island, Northern, and Interior) who worked together to address foundational questions related to the project. As a result, three key decisions were made:

The existing Fraser Health Palliative Symptom Management Guidelines would be the primary source document for revision.

The AGREE II and AGREE II – Global Rating Scale⁴ would be the principal tools used by the Clinician Review Panel through Phase 2.

Although the committee reinforced the necessity for a holistic approach to care, the scope of this project would be limited to end of life symptoms within the physical domain.

In addition, decisions were made outlining the scope of the project including; the audience, care setting, and patient population. The audience for the guidelines was determined to be nurses and physicians without palliative specialization, working with adults with any life-limiting illness, in any care setting (Ideally, with 24-hour access to palliative specialist consultation). The scope was further defined to exclude refractory symptom management or health authority specific protocols such as pre-printed orders.

At completion of Phase 1, an update and report of key decisions was sent to each health authority and the project sponsor.

Phase 2 Literature review, writing and revisions (July 2016 – Aug 31, 2017)

The literature review included sources from 2012-2016, utilizing a modified GRADE⁵ methodology to determine the strength of practice recommendations. Each guideline had internal review amongst members of the writing team and the project lead before being released to the clinician review panel. The guidelines were reviewed from many perspectives and then revised based on multiple feedback sources (Figure 1: Phase 2 process summary).

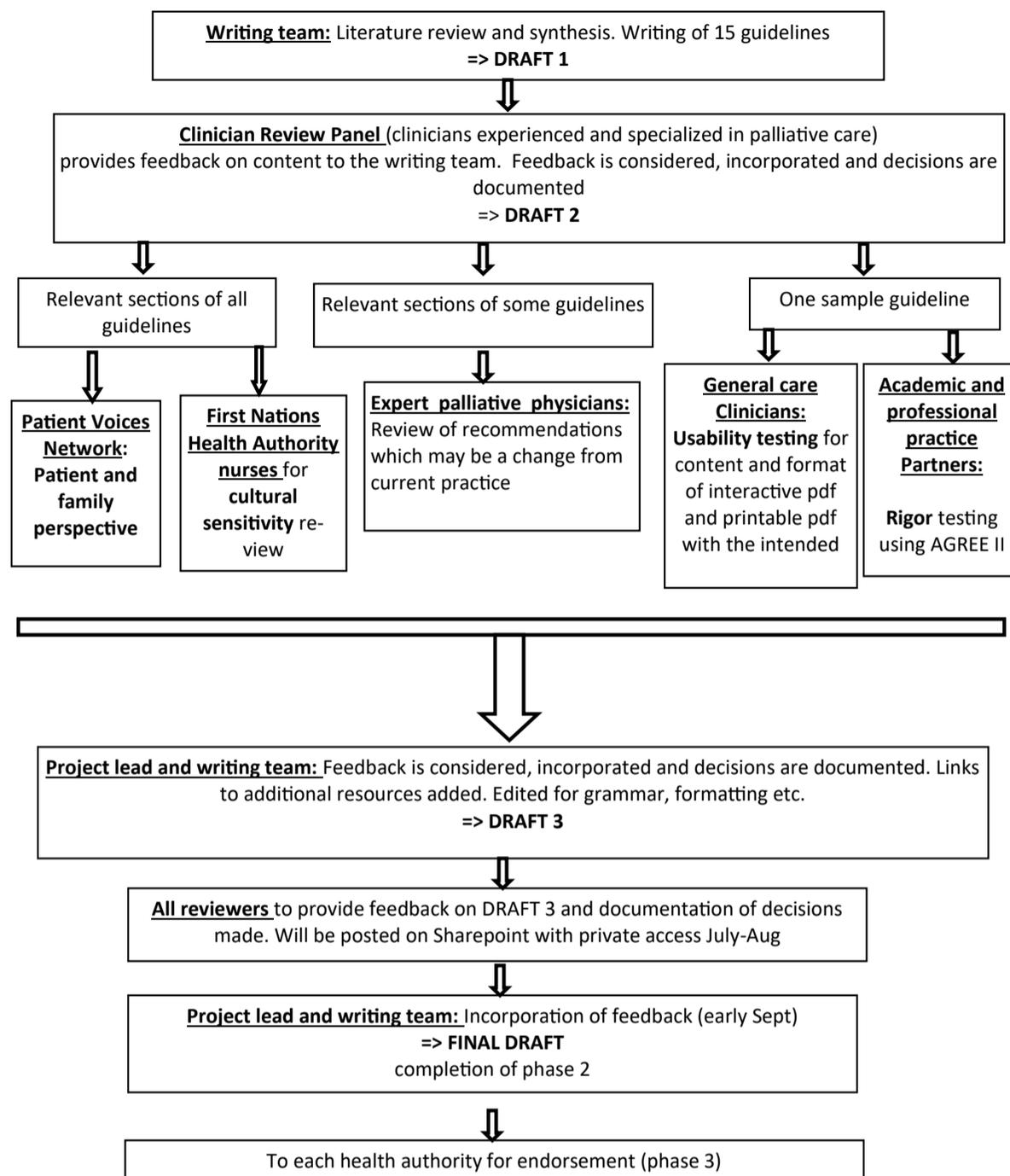
Phase 3 Health authority endorsement and reporting (Sept 1-Dec 23, 2017)

Phase 3 consists of each Steering Committee member putting the guidelines through their health authority's process for adopting new best practice guidelines. Assuming most health authorities endorse the guidelines for clinical use, the project will be complete. The guidelines will then be housed on the BC Centre for Palliative Care website. The anticipated release is at the end of November 2017.

4 Brouwers M, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, Fervers B, Graham ID, Grimshaw J, Hanna S, Littlejohns P, Makarski J, Zitzelsberger L (2010). AGREE II: Advancing guideline development, reporting and evaluation in healthcare. *Can Med Assoc J. Dec 2010; 182:E839-842; doi:10.1503/090449*

5 Goldet, G. and Howick, J. (2013), Understanding GRADE: an introduction. *Journal of Evidence-Based Medicine*, 6: 50–54. doi:10.1111/jebm.12018

Figure 1: Phase 2 process summary



For more detail, please contact Kathleen Yue, Project Lead kyue@bc-cpc.ca

CLINICIAN INTRODUCTION TO THE B.C. PALLIATIVE SYMPTOM MANAGEMENT GUIDELINES

The B.C. Palliative Symptom Management Guidelines were developed to support clinicians to provide effective symptom management for patients with life-limiting illness without a referral to a palliative specialist. Using this reference, we hope you will feel both confident and competent to care for patients and families, enabling them to receive most care from their trusted primary care providers. Each health authority has access to some level of palliative consultation services for advice, coaching and mentorship as well as courses and workshops to strengthen your skills. Please find links to consultation services in the “Additional resources” section of each guideline.

There were several key decisions made about the scope of these guidelines you may find helpful to understand:

1. Symptoms chosen for inclusion were:
 - a. Physical in nature (e.g. spiritual distress was excluded);
 - b. Common to more than one life-limiting illness (e.g. cancer-specific symptoms were excluded).
2. All care settings were included. To support decision making, each of the non-pharmacological interventions is categorized as “available in the home and residential care facilities” or “requiring additional equipment or admission to acute care”.
3. Specific protocols, pre-printed orders, or clinical tools were excluded as they may vary between health authorities.
4. While we anticipate that allied health professionals will find these guidelines useful, they were written with physicians and nurses in mind.
5. Two formats of the guidelines are available; a printable pdf and an interactive pdf (available at the BC Centre for Palliative Care website).

You will notice that the guidelines all have the same structure, this was carefully refined with much feedback. Our intent is to lead you through a process similar to your current practice, with a few modifications to reflect the context of palliative care. We refer to the patient and family as the unit of care (family is whoever the patient finds supportive, regardless of the social relationship).

The standard format

1. Definition
2. Prevalence
3. Impact
4. Standard of care

Step 1 | **Goals of care conversation**

Step 2 | **Assessment**

Using Mnemonic O, P, Q, R, S, T, U and V⁶

Physical assessment

Diagnostics

Step 3 | **Determine possible cause (s)**

Principles of management (a summary of key items in the guideline)

Step 4 | **Interventions**

Legend for use of bullets

Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence using a modified GRADE process.

Non-pharmacological interventions

Pharmacological interventions

Patient and family education

5. Appendix A – Additional Resources for management of symptom

Resources specific to the symptom

General resources

Resources specific to health authority or region

Resources specific to patient population

6. Appendix B - Underlying causes of symptom in palliative care

7. Appendix C – Medications for management of the symptom

8. Appendix D – Management algorithm

9. Appendix E – Extra resources or assessment tools

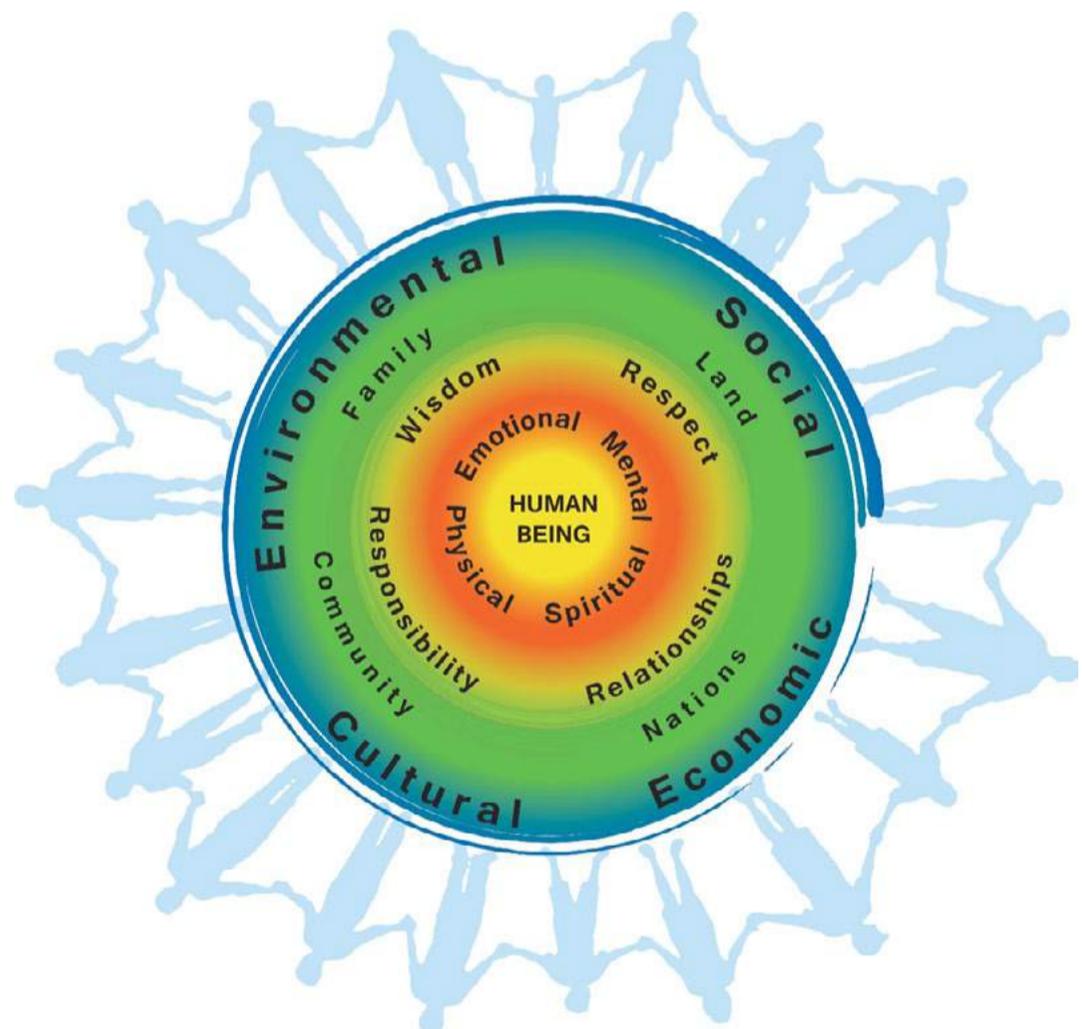
6 Health F. Symptom Guidelines: Hospice Palliative Care, Clinical Practice Committee; 2006 [Available from: <http://www.fraserhealth.ca/health-professionals/professional-resources/hospice-palliative-care/>]

FIRST NATIONS PERSPECTIVE ON HEALTH & WELLNESS

When deciding which symptoms to include in the scope of this project, the Steering Committee chose to include only symptoms directly in the physical facet of life. We included symptoms such as constipation and excluded anxiety, depression and existential distress. The Steering Committee struggled with this decision, as we all agreed it is critical to care for people as holistic human beings, and not to separate them into components. However, two factors influenced this decision: we needed to limit the project's scope to what was achievable with existing resources; and we realized that non-physical distress may not be best classified as a "symptom" per se. To address the other facets of health, we included assessment questions and interventions about non-physical concerns such as anxiety.

We consulted with care providers and members of First Nations communities to try and understand the potential impacts of each physical symptom on the spiritual, emotional and mental facets. Their suggestions have been incorporated into the guidelines, especially in the assessment questions, which include questions about cultural and spiritual values. Many suggestions are applicable for other cultures and beliefs as well, within the overall approach of seeking to understand without judgement.

The "wellness wheel" was the lens through which we viewed health throughout the development of the guidelines. We recognize that a human being can be well within one facet of life while being unwell in another facet. For example, one can be spiritually at peace while physically dying.



First Nations Health Authority. (2014). *First Nations Perspective on Health and Wellness*. Used with permission.

For a further description: <http://www.fnha.ca/wellness/wellness-and-the-first-nations-health-authority/first-nations-perspective-on-wellness>

We learned from our First Nations health partners that some symptoms have spiritual significance, for example, dyspnea may be interpreted not just a sensation physical discomfort, rather as a lack of the essential element of air, which is needed for wellness.

Another example is how a professional trained in western medicine may interpret visions of passed loved ones as a hallucination, whereas some First Nations' people would see this as a needed part of the passing over process. Without this insight, a medical professional may attempt to remove these visions with medication, possibly preventing the comforting presence of loved ones.

We are indebted to our health partners for helping us to appreciate the impact of past trauma, for example, how interventions for constipation may re-traumatize those with past sexual abuse. Also, for insights about the significance of remaining within ones' community and being allowed to utilize traditional remedies and participate in spiritual practices.

The guidelines are much richer because of the health partners' thoughtful input. For future revisions and updates, we recommend including patient and family representatives of other cultures as well as First Nations.

B.C. INTER-PROFESSIONAL PALLIATIVE SYMPTOM MANAGEMENT GUIDELINES: A RESOURCE FOR B.C. - ACKNOWLEDGEMENTS

We are so thankful for the many partners who contributed to these guidelines, making it a true collaborative effort we can all be proud of.

A special thank-you to the original authors of the Fraser Health Hospice Palliative Care Program Symptom Management Guidelines http://www.fraserhealth.ca/media/HPC_SymptomGuidelines_Authors.pdf. The Fraser guidelines have been adapted and adopted in several B.C. health authorities and served as the foundation for this work.

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Definition

Step 1 - Goals of care

Step 2 - Assessment

Step 3 - Possible causes

Principles of management

Step 4 - Interventions

Bullet legend

Non-pharmacological

Pharmacological

Patient and family education

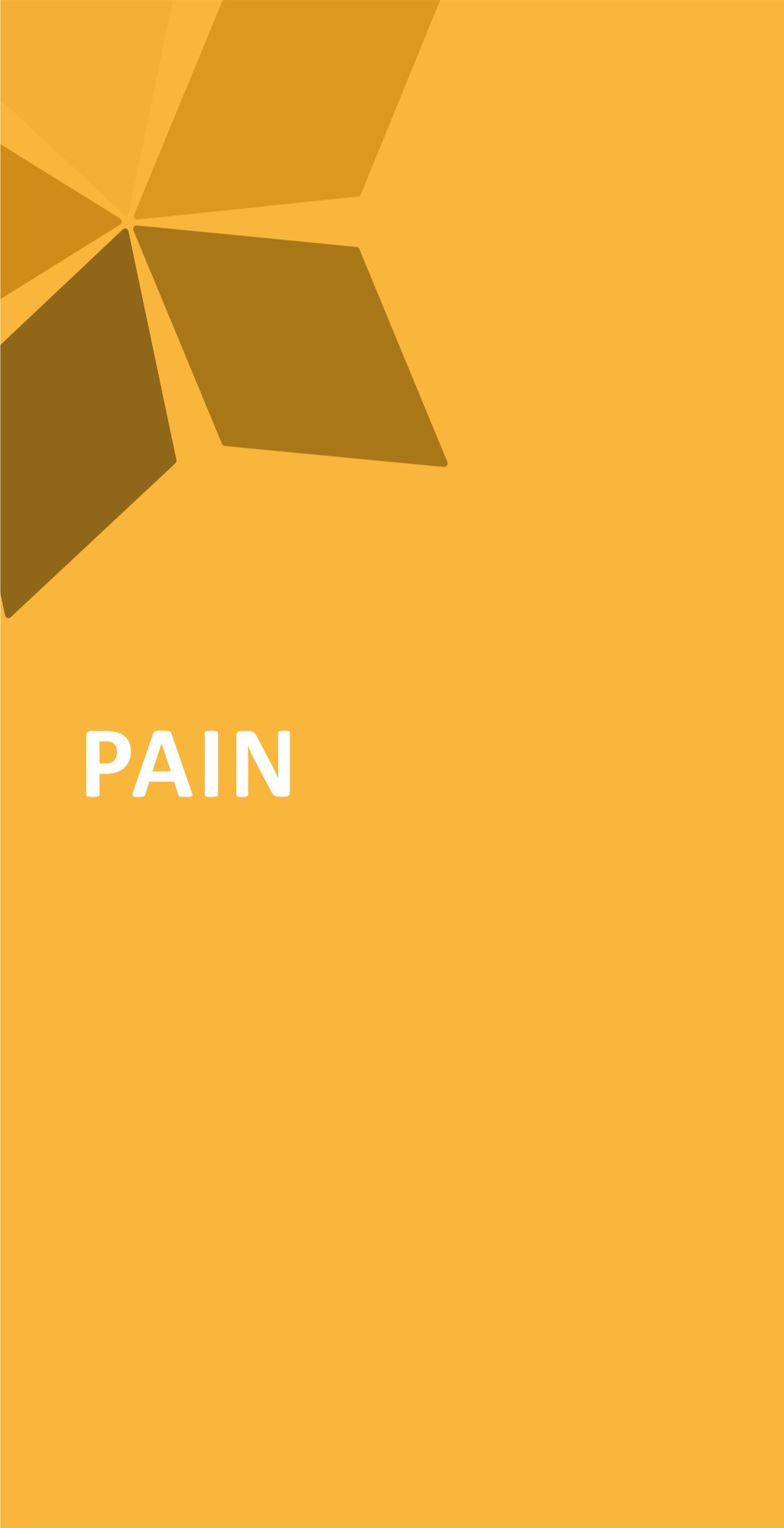
Additional resources

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Extra tools

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PAIN

DEFINITION

Definition

Step 1 - Goals of care

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Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.¹ This guideline does not address management of chronic pain. However, those with chronic pain may have acute pain as their disease advances which is addressed in this guideline.

Nociceptive pain arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors.¹

Neuropathic pain is caused by a lesion or disease of the somatosensory nervous system.¹ It may be associated with abnormal sensations.

Hyperalgesia is an increased perception or experience of painful stimuli.

Allodynia is the experience of pain induced by non-painful stimuli.

Dysesthesias are uncomfortable sensations that are perceived as abnormal and described using terms such as “burning”, “shock-like” or “electrical”. All three are indicative of neuropathic pain mechanisms.⁷⁰

Mixed pain has both nociceptive and neuropathic components.²

Total Pain, a term used often in palliative care, describes the multidimensional factors that contribute to the patient’s experience of pain and suffering.^{3,4}

Background pain is pain present for twelve or more hours per day during the previous week, or would be present if not taking analgesia.⁶⁶

Breakthrough pain (BT) is a transient exacerbation of pain that occurs either spontaneously, or in relation to a specific predictable or unpredictable trigger, despite relatively stable and adequately controlled background pain.⁶⁶ Different subtypes of breakthrough pain:

Incident pain is precipitated by a movement or a voluntary action, and is predictable or expected.^{67, 68}

Spontaneous pain is not related to an identifiable precipitant, and so is unpredictable in nature.⁶⁶

End-of-Dose Failure describes an exacerbation of pain that occurs prior to the next dose of the background analgesic, and reflects declining levels of the background analgesic.⁶⁹

Breakthrough Dose (BTD) is an additional dose used to control breakthrough pain. It does not replace or delay the next routine dose. BTD is also known as a rescue dose.⁴⁴

Titration: Adjustments of analgesics to improve pain control and to minimize adverse effects

Total Daily Dose (TDD) is the 24 hour total of a drug that is taken for regular and breakthrough doses combined.⁴⁴

Definition

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PREVALENCE

Pain at end of life is highly prevalent among all patient groups regardless of primary diagnosis.⁵ Although pain can be well or completely controlled in up to 90% of patients using standard therapies in accordance with well-publicized guidelines,⁶⁻¹³ pain still remains under-recognized and undertreated in many patient groups.¹⁴

IMPACT

Unrelieved pain has a significant impact on the physical, emotional and functional wellbeing of patients and caregivers.¹⁵⁻¹⁸ Access to appropriate assessment and treatment of pain should be considered an ethical imperative and human right.^{19, 20}

STANDARD OF CARE

Step 1 | Goals of care conversation

Determine goals of care in conversation with the patient, family and inter-disciplinary team. Refer to additional resources (Additional Resources for Management of Pain) for tools to guide conversations and required documentation. Goals of care may change over time and need to be reconsidered at times of transition, e.g., disease progression or transfer to another care setting.

Step 2 | Assessment

Definition

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Step 2 - Assessment

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Bullet legend

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- Perform a comprehensive pain assessment for each pain reported.
- For those unable to communicate verbally, assess for pain by non-verbal indicators, such as restlessness and rigidity, grimacing, and distressed vocalizations such as moaning and repeated calling out.²¹
- Use an observational pain rating scale to assess behavioral indicators of pain such as the Pain Assessment in Advanced Dementia Scale (PAINAD) Scale (see [Additional resources for management of pain](#) for link).²²

Pain Assessment: Using Mnemonic O, P, Q, R, S, T, U and V90

| Mnemonic Letter | Assessment Questions <i>Whenever possible, ask the patient directly. Involve family as appropriate and desired by the patient.</i> |
|-------------------------------|--|
| O nset | When did it begin? How long does it last? How often does it occur? |
| P rovoking /Palliating | What brings it on? What makes it better? What makes it worse? |
| Q uality | What does it feel like? Can you describe it? If unable to describe, ask is the pain sharp, dull, aching, burning, or do they experience pins and needles? |
| R egion/Radiation | Where is it? Does it spread anywhere? Use a body map to illustrate location and number of pain areas (see Pain extra resources or assessment tools for body map link). |
| S everity | How severe is this symptom? What would you rate it on a scale of 0-10 (0 being none and 10 being the worst possible)? Right now? At worst? On average? How bothered are you by this symptom? Are there any other symptom(s) that accompany this symptom? If the patient has difficulty using a numerical rating scale use an alternative such as the visual analogue scale (VAS) or verbal rating scale (VRS) (link in Pain extra resources or assessment tools). ^{1, 3, 23} |
| T reatment | What medications and treatments are you currently using? Are you using any non-prescription treatments, herbal remedies, or traditional healing practices? How effective are these? Do you have any side effects from the medications and treatments? What have you tried in the past? Do you have concerns about side effects or cost of treatments? |
| U nderstanding | What do you believe is causing this symptom? How is it affecting you and/or your family? What is most concerning to you? What are your beliefs about opioid/narcotic medications? (See Pain extra resources or assessment tools for responses to common misconceptions.) |
| V alues | Are you having to make compromises such as decreasing activities or enduring side effects to deal with your pain? What overall goals do we need to keep in mind as we manage this symptom? What is your acceptable level for this symptom (0-10)? Are there any beliefs, views or feelings about this symptom that are important to you and your family? |

Step 2 | Assessment continued on [next page](#)

Step 2 | Assessment *continued*

Symptom Assessment: Physical assessment as appropriate for symptom

Definition

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Completion of a comprehensive pain assessment will determine the etiology and type of pain to enable appropriate treatment for each type/location of pain reported. Ongoing documentation of assessment findings, treatment plan and patient response is essential to find trends for effective team communication and optimal care. **Place in a readily visible and consistent location.**

Diagnostics: consider goals of care before ordering diagnostic testing

Pain etiologies, types and sites will determine investigation and imaging requirements.

First, determine if an emergency situation exists. **If so, refer the patient immediately to the acute hospital setting** for further investigations and treatment of the underlying cause while proceeding to treat the pain.

Pain emergencies

Spinal cord compression, bone fracture or impending fracture of weight-bearing bone, infection/abscess, obstructed or perforated viscus, an ischemic process, or superior vena cava obstruction.²³

Step 3 | Determine possible causes and reverse as possible if in keeping with goals of care (For more details, see [Underlying causes and possible medications for pain in palliative care](#)):

Assess each reported pain fully, based on pathophysiology, before discussing treatment options.³⁹

PRINCIPLES OF MANAGEMENT



When considering a management approach, always balance burden of a possible intervention against the likely benefit (e.g., does the intervention require transfer to another care setting?).

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- Pain rarely occurs in isolation in patients with advanced disease.^{4, 25}
- Conduct a multidimensional assessment for prompt recognition and treatment of pain to improve comfort and quality of life.^{1, 26}
- Educate patients about their pain and involve them in decision-making about their pain management plan.^{2, 27-29}
- Reassess pain at regular and frequent intervals: at expected peak action time of analgesic, following the start of new treatment, with each new report of pain, with any change in the presentation of pain, and when pain is not relieved by previously effective strategies.^{30, 31}
- Seek consultation if pain is not improving with titration, adequately relieved within 72 hours, or for pain that is not managed after applying standard analgesic guidelines and interventions.
- Assess and treat other symptoms to maximize patient comfort.
- The 3 practices of assessment, documentation and decision making need to be routinely linked for a consistent approach to pain management.⁸⁹
- Clinicians are encouraged to consider the use of traditional, Western and non-pharmacologic strategies to optimize pain management.³²
- The concept of total pain reminds us that a unilateral pharmacological approach will not be adequate to address the multiple factors that influence pain and suffering. An inter-professional approach to pain management is recommended whenever possible.³³

Step 4 | Interventions

LEGEND FOR USE OF BULLETS

Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence, using a modified GRADE process.

| | |
|--|--|
|  | Use with confidence: recommendations are supported by moderate to high levels of empirical evidence. |
|  | Use if benefits outweigh potential harm: recommendations are supported by clinical practice experience, anecdotal, observational or case study evidence providing low level empirical evidence. |
|  | Use with caution: Evidence for recommendations is conflicting or insufficient, requiring further study |
|  | Not recommended: high level empirical evidence of no benefit or potential harm |

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Non-pharmacological pain strategies that may be available in the home or residential care facilities include but are not limited to:

-  **Physical:** such as physio, exercise, massage, positioning, application heat/cold. Note: use with caution with frail elderly.
-  **Psychological:** such as relaxation, meditation, cognitive therapy.³²
-  **Relevant spiritual and cultural practices.**

For additional information on non-pharmacological interventions, see National Centre for Complementary and Alternative Medicine (link in [Additional resources for management of pain](#)).

Interventions requiring additional equipment or transfer to acute care

Transcutaneous Electrical Nerve Stimulation (TENS), acupuncture, acupressure.

Specialized Medical therapies include (All require consultation with palliative specialist for appropriate referrals):

- Palliative radiation
- Palliative surgery
- Neuroaxial analgesia
- Cementoplasty

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1) Considerations before choosing an analgesic

-  Match pain causes to drug treatment choice considerations (see [Medications for management of pain based on type of pain](#) for possible causes).
-  Use patient specific goals and preferences to aid drug selection.
-  Review health performance status, medical conditions, organ impairments, allergies. Determine if they may limit drug options. Consider drug limiting factors including interactions, concerns about medication use, adherence, risk of misuse or abuse.
-  Discuss and resolve concerns about tolerance, fears, addiction and side effects.³⁹ (See [Pain extra resources or assessment tools](#) - Response to Common Misconceptions About Opioid Analgesics)
-  Ensure patient access to prescribed medications, considering cost and ability to access medications in their care setting. Activate drug benefit coverage for BC PharmaCare Palliative Care Benefits program appropriately.
-  Assess and actively treat other symptoms that can potentially make pain perception worse, such as nausea or constipation. Refer to other management guidelines for more information.

2) Assess substance/opioid misuse risk

-  All patients being considered for opioid therapy should be evaluated for substance use disorder.⁴⁰ Prescribers should be familiar with the BC College of Physicians Professional Standards and Guidelines: Safe Prescribing of Drugs with Potential for Misuse/Diversion (link in [Additional resources for management of pain](#))⁴¹ However, **the College recognizes that these standards may not apply to treatment of palliative, nursing home and end-of-life patients.**⁴¹ If opioid misuse or abuse expected, complete a risk assessment prior to treatment.³⁰ The Opioid Risk Tool is one of several useful tools ([Pain extra resources or assessment tools](#) for link).⁴² Patient self-reports of substance misuse are variable and consideration of urine drug testing has been recommended.⁴⁰

Treatment with an opioid analgesic is not contraindicated in a patient with a history of substance use disorder but requires a comprehensive treatment plan.⁴⁰

3) Initiation of analgesics (see [Medications for management of pain based on type of pain](#) for detailed pharmacological information and [Additional resources for management of pain](#) for additional resources such as use of fentanyl patch and equianalgesic tables)

-  Integrate non-pharmacological treatments and adjuvant analgesics concurrent with analgesics for all levels of pain: mild, moderate or severe.
-  Treatment choices are guided by pain intensity on a scale with 0-10 with 0 being none and 10 being the worst possible; **however, when pain is expected to worsen, choosing from options for more intense pain may avoid a future medication switch.**⁴⁴

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Mild pain (patient rating of 1 to 4/10)

 Acetaminophen or non-steroidal anti-inflammatories (NSAIDs).

 Acetaminophen and NSAIDs may be used together for mild acute pain.⁴³

Moderate pain (patient rating of 5 to 6/10)

 Acetaminophen combined with oxycodone, tramadol, or tapentadol.⁴⁵⁻⁴⁸
Ensure acetaminophen daily intake limits not exceeded.

 Switch from compound immediate release products to a single sustained release opioid.^{50,51}

 Switching from codeine to other opioids has shown improvement in pain control.⁵⁰

 **Avoid codeine.** It is not preferred due to:

- Unpredictable safety and efficacy due to variable liver metabolism amongst individuals.^{46, 49, 87}
- Possible interactions with other medications causing variable metabolism.⁸⁸
- It is often not sufficient for cancer pain and as intensity increases, a switch will need to be made.

Severe pain (patient rating of 7 to 10/10)

 First line options are oral morphine, hydromorphone or oxycodone. They are similarly effective for cancer pain.^{45, 52-54}

 Use opioids with the lowest cost when all other considerations are equal.⁴⁵

 Consider hospital or inpatient hospice admission for acute, severe pain or pain crisis.³⁰

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Initiation of Analgesics Clinical Review Points (also see Fraser Health Opioid principles link in [Additional resources for management of pain](#))

-  **START LOW** – Start with low doses, especially with impaired renal or liver function and in the elderly.
-  **GO SLOW** - Titrate doses gradually to analgesic response or until patient experiences unacceptable side effects. (See titration section below). May begin with less frequent dosing (e.g., q6h instead of q4h).
-  **BY MOUTH** - While the oral route is most common as the safest and least invasive administration method, other routes (IV, subcutaneous, rectal, transdermal, transmucosal) can be used as indicated to maximize patient comfort.^{55, 57}
-  **BY THE CLOCK** - Regular/fixed administration schedule, such as every 4 or 6 hours, rather than only “on demand”,²⁴ including waking from sleep for a scheduled dose. Once pain control achieved, switch to long acting agents to improve compliance and sleep.⁵⁵
-  **PLAN FOR ADVERSE EFFECTS** – Anticipate, monitor and manage analgesic adverse effects, including starting laxatives proactively.
-  **PLAN FOR BREAKTHROUGH PAIN** - When starting an opioid, use immediate release with breakthrough doses (BTD) until dose is stabilized to enable timely and effective titration.^{44, 46, 55}

Breakthrough dosing

-  Breakthrough doses are generally 10% of the total regular daily opioid dose.⁵⁶
-  Use immediate release opioids every hour orally or every 30 minutes subcutaneously PRN
-  Use of the same opioid for breakthrough pain doses and the regularly scheduled opioid improves the ease and clarity for determining future dose titrations.
-  Reassess when 3 or more breakthrough doses used per 24 hours (See titration section below).

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4) Titration: Adjustments to improve pain control and to minimize adverse effects

-  Use practice tools to monitor pain rating, adverse effects, and track patient goal attainment. A suitable numerical or descriptive pain rating scale should be used consistently.
-  Follow sedation levels using a tool such as the Pasero Opioid-Induced Sedation Scale⁷⁸ (see [Pain Extra resources or assessment tools](#)), especially during titration of opioid doses.
-  Individualize dosing readjustments balancing effectiveness and tolerability.
-  Following selection of a starting opioid dose, adjustment is almost always required.⁴⁶
-  Titrate with caution in patients with risk factors such as decreased renal/hepatic function, chronic lung disease, upper airway compromise, sleep apnea, or poor performance status.³⁰

Titration

1. Calculate total daily dose (TDD) for the past 24 hours
TDD = Regular + all BTD^{44, 58}
2. Regular dose q4h for the next 24 hours = past **TDD ÷ 6**
3. Breakthrough dose (BTDD) = **new regular dose × 10%⁴**
Increase the opioid BTDD proportionately whenever the regular dose is increased.⁴⁴

-  Adjustment may require a dose adjustment of both the regular dose as well as the BTDD.
-  Dose adjustments should not be made more frequently than every 24 hours.⁴⁴ However, severe or crisis pain may require more aggressive titration.⁴⁴
-  The rapidity of the dose escalation should be related to the pain severity, expected onset and duration of analgesics, and ability to monitor during dose titration.³⁰
-  Individualized dosing readjustments can use fixed dose increases, e.g., a 30-50% opioid dose increase, or base increased regular analgesic dose on quantity of BTDD.
-  Adverse effects from opioids can be managed by dose reduction, changing to a different opioid or route of administration, or symptomatic management, e.g., anti-emetic use.⁵⁹
-  Impaired swallowing capacity can require a conversion of oral opioids to subcutaneous or intravenous routes; reduce parenteral doses by half for chronic pain, reflecting potency differences.⁴⁴
-  Monitor for excessive opioid doses; effects often are sedation or confusion.
-  Addressing opioid-induced neurotoxicity will require strategies including lowering doses, a switch (rotation) to a different opioid, hydration and consultation. Refer to the Twitching/Myoclonus/Seizures guideline for myoclonus management.

See additional resources in [Additional resources for management of pain for pain and opioid management guidelines](#).

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5) Adjuvant Analgesics to improve pain control

-  Optimize the opioid regimen before introducing an adjuvant analgesic in cancer pain.⁶²
-  Adjuvant analgesics are medications that have a primary indication other than pain, but have analgesic effects in some types of painful conditions.⁶⁰ They include: anticonvulsants, antidepressants, corticosteroids, muscle relaxants, topical NSAIDs/opioids, bone modifying drugs. See [Medications for management of pain based on type of pain](#) for detailed medication list.
-  Use appropriate adjuvant analgesics at any pain severity level.⁶¹
-  Select based on predominating pain type, symptoms, comorbidities, supporting clinical evidence, potential adverse effects, drug interactions, ease of administration and cost.
-  The adjuvant analgesic with the greatest benefit and least risk should be administered as first-line treatment.⁶² Often this is an anticonvulsant such as gabapentin, or an antidepressant such as nortriptyline for treatment of cancer-related neuropathic pain.⁶³
-  Doses should be increased until the analgesic effect is achieved, adverse effects become unmanageable, or the conventional maximum dose is reached.³⁰ Reassess regularly and taper or discontinue ineffective medications.^{30, 56}
-  Consider combination therapy with two or more drugs in the event of partial response to single drug therapy.⁶⁴ However, avoid initiating and titrating several adjuvants concurrently.⁶² Opioid rotation within an adjuvant combination is suggested as a further progressive pain strategy.⁶⁵

6) Utilize Consultation Services – when to consider calling for help!

- For **unrelieved pain**. Pain should improve on titration within 72 hours.
- For **rapidly escalating pain**, not responding to opioid titration, to point of concern or suffering.
- **Specific situations** such as: unmanageable adverse effects, toxicity, special patient populations (e.g., moderate to severe renal or liver impairment), safety concerns, substance abuse.
- **Use of methadone, ketamine, lidocaine or interventional treatment strategies**. See [Additional resources for management of pain for additional resources for prescription of methadone for analgesia](#); these medications can be prescribed by family physicians.
- Need of **qualified specialists** such as pain specialists, oncologists, orthopedics, anaesthesiologists.

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- Instruct patients/families to contact clinician if pain or side effects worsen.
- Encourage patients to report their pain.^{3, 27, 34-36} Inform patients they have the right to receive adequate pain management. Reassure them their report of pain will be believed and acted upon.³⁷
- If patient and family disagree about the use of pain medication, explore their understanding and come to agreement, especially if family members are administering analgesics.
- Accurate and reliable information should be given regarding opioid treatment; detect and correct false beliefs or misunderstandings that may affect adherence to the treatment, its effectiveness, and patient safety.³⁸ (see [Pain extra resources or assessment tools](#) for detailed responses to common misconceptions.)
- Give an explanation for the cause of each pain and reassurance that pain can usually be very well controlled.²³
- Identify the three simple stepwise goals for pain management:³³
 - A good night's sleep.
 - Pain control during the day while at rest.
 - Pain control when active and ambulatory.
- Describe the 3 common side effects for opioid naïve patients: cognitive (confusion or sedation), nausea and constipation. Explain that cognitive and nausea side effects commonly improve and disappear in 3 to 7 days. Elicit level of patient and family willingness to tolerate short term side effects during the titration phase. Constipation will need ongoing management.
- Teach patients and families how to use an appropriate pain assessment tool, and encourage patients to keep a pain diary (see [Additional resources for management of pain](#) for link) and record scheduled and breakthrough analgesia usage.
- Explain how to use pain medication effectively.²⁸
 - What the medications are and why they have been prescribed.
 - How and when they should be taken.
 - Potential adverse effects and how they can be managed if they occur.
 - Medication safety processes.
 - How prescriptions are filled.
 - Safe handling, storage, and pharmacy take-back disposal of analgesics, particularly opioids.³⁰

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Resources specific to pain

- BC College of Physicians Professional Standards and Guidelines: Safe prescribing of drugs with potential for misuse/diversion
→ <https://www.cpsbc.ca/files/pdf/PSG-Safe-Prescribing.pdf>
- College of Physicians and Surgeons of British Columbia Controlled Drug Resources
→ <https://www.cpsbc.ca/programs/drug-programs/prp/prp-guidelines>
- College of Physicians and surgeons of British Columbia: Methadone for analgesia (Click on “Resources” - includes an online module)
→ <https://www.cpsbc.ca/programs/drug-programs/mmp>
- National Centre for Complementary and Alternative Medicine
→ <https://nccih.nih.gov/health/integrative-health#types>
- Fraser Health: Opioid Principles Jan 2016
→ http://www.fraserhealth.ca/media/HPC_SymptomGuidelines_Opioid.pdf (includes use of the World Health Organization (WHO) analgesic ladder, guidance for Fentanyl patches, titration and equi-analgesic tables)
- Pain Assessment in Advanced Dementia (PAINAD)
→ <http://bcbpsd.ca/docs/part-1/Final%20Provincial%20PAINAD%20Scale.pdf>

General Resources

- **Provincial Palliative Care Line** – for **physician** advice or support, call **1 877 711-5757** In ongoing partnership with the Doctors of BC, the toll-free Provincial Palliative Care Consultation Phone Line is staffed by Vancouver Home Hospice Palliative Care physicians 24 hours per day, 7 days per week to assist physicians in B.C. with advice about symptom management, psychosocial issues, or difficult end-of-life decision making.
- BC Centre for Palliative Care: Serious Illness Conversation Guide
→ <http://www.bc-cpc.ca/cpc/>
- BC Guidelines: Palliative Care for the Patient with Incurable Cancer or Advanced Disease
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care>
- BC Palliative Care Benefits: Information for prescribers
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program>
- National Centre for Complementary and Alternative Medicine (NCCAM) for additional information on the use of non-pharmacological interventions
→ <https://nccih.nih.gov/>
- Canadian Association of Psychosocial Oncology: Pan-Canadian Practice Guideline: Screening, Assessment and Management of Psychosocial Distress, Depression and Anxiety in Adults with Cancer
→ http://www.capo.ca/wp-content/uploads/2015/11/FINAL_Distress_Guideline1.pdf

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- Fraser Health psychosocial care guideline
→ <https://www.fraserhealth.ca/media/psychosocial%20care.pdf>

Resources specific to health organization/region

- Fraser Health
→ <http://www.fraserhealth.ca/health-professionals/professional-resources/hospice-palliative-care/>
- First Nations Health Authority
→ <http://www.fnha.ca/>
- Interior Health
→ <https://www.interiorhealth.ca/YourCare/PalliativeCare/Pages/default.aspx>
- Island Health
→ http://www.viha.ca/pal_eol/
- Northern Health
→ <https://www.northernhealth.ca/Professionals/PalliativeCareEndofLifeCare.aspx>
- Providence Health
→ <http://hpc.providencehealthcare.org/>
- Vancouver Coastal Health
→ <http://www.vch.ca/your-care/home-community-care/care-options/hospice-palliative-care>

Resources specific to patient population

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians
→ <https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf>
- ALS Society of British Columbia 1-800-708-3228
→ www.alsbc.ca
- BC Cancer Agency: Symptom management guidelines
→ <http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management>
- BC Renal Agency: Conservative care pathway and symptom management
→ <http://www.bcrenalagency.ca/health-professionals/clinical-resources/palliative-care>
- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management
→ <http://www.bcheartfailure.ca/for-bc-healthcare-providers/end-of-life-tools/>

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- Canuck Place Children's Hospice
 - <https://www.canuckplace.org/resources/for-health-professionals/>
 - 24 hr line – 1.877.882.2288
 - Page a Pediatric Palliative care physician – 1-604-875-2161 (request palliative physician on call)
- Together for short lives: Basic symptom control in pediatric palliative care
 - http://www.togetherforshortlives.org.uk/professionals/resources/2434_basic_symptom_control_in_paediatric_palliative_care_free_download

UNDERLYING CAUSES AND POSSIBLE MEDICATIONS FOR PAIN IN PALLIATIVE CARE⁷²

Algorithm created by Dr Nicola Macpherson, MD FRCPC (Anesthesiology), DABHPM. Hospice Palliative Care Physician, Fraser Health, British Columbia, Canada. Adapted with permission

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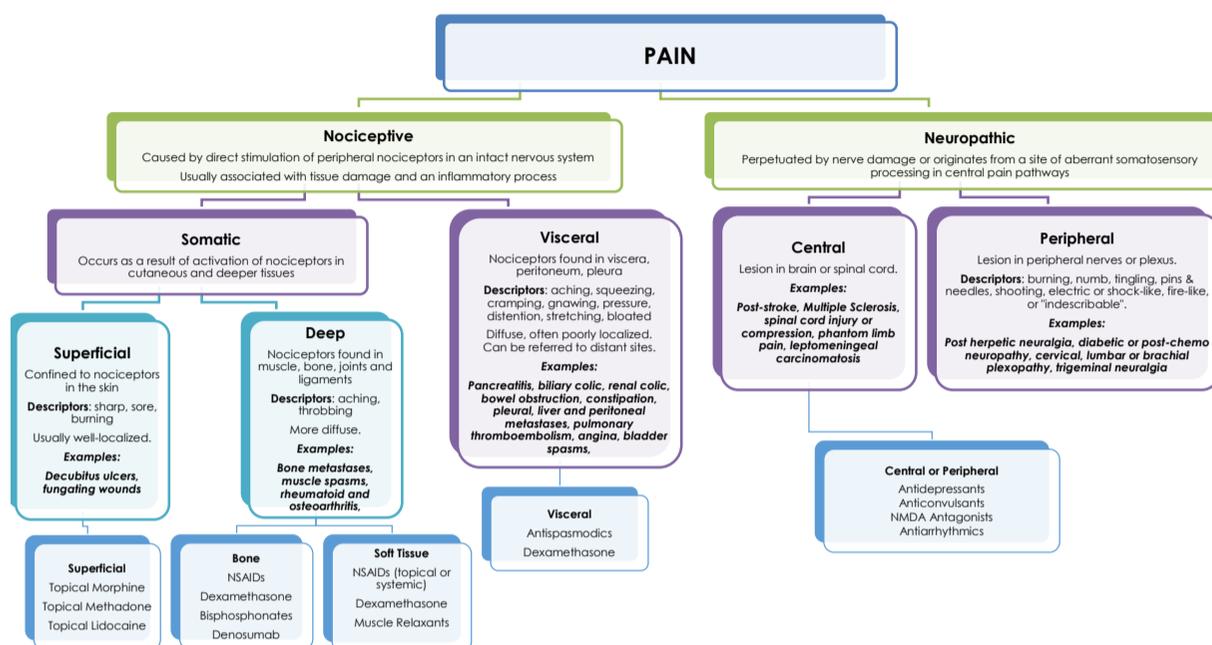
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| Drug, Action | Dose, Therapeutic Range ⁷³ | Onset, Adverse Effects, Precautions and Dosing Concerns ⁷³⁻⁷⁵ |
|-------------------------|--|---|
| 1. Pain | | |
| Acetaminophen | 500 to 1g PO, PR q6h to q4h 650 to 1300 mg SR PO q8h | Caution in renal impairment and severe hepatic impairment, particularly when associated with alcohol dependence and malnutrition. Maximum 4 g per day or 3 g in the elderly. ^{76,77} |
| NSAIDs | | Avoid in frail elderly, cardiac, renal and hepatic dysfunction, or active peptic ulcers. |
| Diclofenac | 50 mg PO, PR q12h or q8h 75 SR PO q12h or 100 mg daily 50 to 100 mg PR q8h | Maximum 150 mg per day |
| Ibuprofen | 400 to 800 mg PO q8h | Maximum 2400 mg per day |
| COX-2 Inhibitors | | Contraindicated if established ischaemic heart disease, peripheral arterial disease or cerebrovascular disease. |
| Celecoxib | 200 to 400 mg PO daily or q12h | Maximum 400 mg per day |
| Meloxicam | 7.5 to 15 mg PO daily | Maximum 15 mg per day |
| Corticosteroids | | Start at a high dose then reduce to a maintenance level. <u>Stop if no response within 7 to 10 days.</u> Taper steroid dose gradually if used for more than 3 weeks or if stopping doses greater than 4 mg per day. |
| Dexamethasone | <u>High Dose:</u> 8 mg PO, SC once daily or twice daily <u>Low Dose:</u> 2 to 6 mg PO, SC daily | Hyperglycemia, anxiety, steroid psychosis, myopathy. Long-term adverse effects are significant; therefore, avoid prolonged use. Avoid concomitant use with NSAIDs. |

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| 2. Superficial Somatic Pain | | |
|---|---|---|
| Topical NSAIDs | | Do not apply on an open wound, or on areas of infection or rash. Apply to affected area up to 4 times per day. |
| Diclofenac Sodium | Apply 1.5% cream topically | |
| Diclofenac Gel | Apply 1.16 to 5% cream topically | |
| Ketoprofen | Apply 5 to 20% cream topically | |
| Topical Opioids | Apply topical morphine 0.1% (1 mg per mL) in hydrogel once to twice daily | The amount of gel applied varies according to the size and the site of the inflammation or ulcer. The topical morphine is kept in place with gauze or a non-absorbable dressing. |
| 3. Deep Somatic Bone Pain | | |
| Bisphosphonates - bone modifying agent | | Adverse effects include: osteonecrosis of the jaw, renal impairment, or hypocalcemia. Transient mild flu-like symptoms for 1 to 2 days may occur after administration. Monitor renal function and calcium with each treatment. <u>Dental review is necessary before initiation.</u> Use with extreme caution in renal impairment, dose adjustment required. |
| Clodronate | 900 mg IV every 4 weeks | |
| | 1600 to 2400 mg PO daily | |
| Pamidronate | 60 to 90 mg IV every 3 to 4 weeks | |
| Zoledronic Acid | 4 mg IV every 4 weeks | |
| Monoclonal Antibody - bone modifying agent | | Monitor calcium levels prior to administration. <u>Dental review is necessary before initiation.</u> No dose adjustment required for renal impairment. |
| Denosumab | 120 mg SC every 4 weeks | |
| 4. Deep Somatic Soft Tissue Pain | | |
| Skeletal Muscle Relaxant | | |
| Diazepam | 2 to 10 mg PO at night | Useful for painful muscle spasm. Adverse effects include drowsiness and ataxia. Caution in elderly patients. |
| Baclofen | 5 mg PO q12h or q8h | Start at 5 mg daily and increase to 15 mg daily in divided doses. Maximum recommended dose 100 mg daily. Monitor liver function tests periodically. Abrupt cessation associated with seizures. Adverse effects include drowsiness. |
| Tizanidine | 2 to 8 mg PO q8h or q6h | Start at 2 mg daily and increase by 2 mg every 3 to 4 days according to response. Maximum recommended total daily dose 36 mg. |

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| 5. Visceral Pain | | |
|-------------------------|-----------------------------------|---|
| Anticholinergics | | |
| Hyoscine butylbromide | 20 mg SC q6h | Monitor for peripheral antimuscarinic effects which may include: blurred vision, dry mouth, constipation and urinary retention. Does not cross the blood brain barrier; therefore, does not cause sedation. Maximum recommended total daily dose 300 mg. |
| | 60 to 120 mg CSCI daily | |
| 6. Neuropathic Pain | | |
| Antidepressants | | First line for neuropathic pain |
| TCAs | | Starting dose 10 to 25 mg at bedtime. Titrate slowly every 3 to 7 days by 10 to 25 mg as tolerated. Target therapeutic dose range 75 to 150 mg daily. Monitor for anticholinergic effects: drowsiness, constipation, dry mouth, urinary retention. Avoid if poor cardiac function, severe prostatic hypertrophy, or glaucoma. Positive effects on mood and sleep may be desirable. |
| Amitriptyline | 75 to 150 mg PO at bedtime | |
| Nortriptyline | 75 to 150 mg PO at bedtime | |
| SNRIs | | Safer and better tolerated than TCAs, but limited evidence of analgesic efficacy. Initiate venlafaxine at 37.5 mg daily for one week. |
| Duloxetine | 60 to 120 mg PO daily | |
| Venlafaxine | 75 to 225 mg PO daily | |
| Anticonvulsants | | First line for neuropathic pain |
| Gabapentin | 300 to 800 mg PO every q8h to q6h | Starting dose 100 to 300 mg at bedtime. Titrate slowly every 1 to 7 days by 100 to 300 mg as tolerated. Target therapeutic dose ranges from 900 to 3600 mg daily in 3 to 4 divided doses. <u>An adequate trial should include 1 to 2 weeks at the maximum-tolerated dose.</u> Monitor for somnolence, dizziness, and ataxia. Slower titration for the elderly or medically frail. Dose adjustment required for those with renal insufficiency. |
| | | Pregabalin |
| Pregabalin | 150 to 300 mg PO q12h | Starting dose 75 mg twice daily. Titrate slowly every 3 to 7 days. Target therapeutic dose ranges from 50 to 150 mg daily in divided doses. Monitor for somnolence, dizziness, and ataxia. Slower titration for the elderly or medically frail. Dose adjustment required for those with renal impairment. |

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| Analgesic Adjuvants for Consideration AFTER Specialist Consultation | | |
|--|--|---|
| NMDA Blockers | | Second line for neuropathic pain |
| | 10 to 50 mg PO q8h to q6h | Starting dose 10 to 25 mg q8h. Titrate in steps of 10 to 25 mg up to a maximum dose of 200 mg q6h. |
| Ketamine | 100 to 500 mg CSCI daily | Start with 100 mg over 24 hours. Increase after 24 hours to 300 mg over 24 hours and further increase to 500 mg over 24 hours if ineffective. Stop 3 days after last dose increment. Monitor for psychomimetic effects. Treat dysphoria with haloperidol, diazepam or midazolam. |
| Local Anesthetic | | Second line for neuropathic pain |
| Lidocaine | 5 to 12.5 mg per kg over 120 minutes IV or SC every 2 weeks OR by continuous infusion | Use with caution in patients with cardiac failure. Dose adjustment required in hepatic or renal impairment. |

† Off-label. PO = by mouth IV = Intravenous, SC = Subcutaneous, TID = three times daily, QID = four times daily ODT = oral dissolving tablet CSCI = continuous subcutaneous infusion.

Prices for prescription drugs may be obtained from BC PharmaCare. The British Columbia Palliative Care Benefits Plan <http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/palliative-formulary.pdf> provides province wide drug coverage for many of the recommended medications– check website to confirm coverage. **Consider price when choosing similarly beneficial medications, especially when the patient / family is covering the cost.**

PAIN MANAGEMENT ALGORITHM

No management algorithm included in this document; however, [Underlying Causes of pain in Palliative Care](#) – Underlying Causes of Pain in Palliative Care contains possible treatments based on cause.

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Body map

→ https://scripts.glosnhs.net/mpqreferralform/body_Pain.htm

Visual analogue scale (VAS)

→ <https://www.painedu.org/Downloads/NIPC/Pain%20Assessment%20Scales.pdf>

The Opioid Risk Tool

→ <http://www.viha.ca/NR/ronlyres/8AF0014E-06D5-4D1A-B922-BD3F985C9B00/0/201011038RiskToolOpioidRiskToolClinicianForm.pdf>

Patient pain diary

→ http://www.virtualhospice.ca/en_US/Main+Site+Navigation/Home/Support/Resources/Books_+Links_+and+More/Symptoms/General+symptoms/Online+Resources/Symptom+Diary.aspx

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Response to Common Misconceptions About Opioid Analgesics^{24, 72}

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| Patient/Family Fears and Misconceptions | Possible Healthcare Professional Responses |
|---|--|
| Fear of Addiction | Opioid addiction in patients with cancer related-pain patients is extremely rare. ^{79, 80} If opioids are abruptly discontinued, a physical withdrawal reaction may occur. This is a normal physiological reaction, not a sign of addiction. This can be prevented by gradually tapering off the medication. |
| Fear of Side Effects | Drowsiness, nausea and constipation commonly occur with the use of opioids. These side effects will be addressed while the pain is being managed. Drowsiness and/or nausea may develop when opioids are started or when the opioid dose is increased, but usually resolves within 3 to 5 days. Constipation will always occur and needs to be anticipated, pro-actively managed, and assessed on an ongoing basis. |
| Fear it Won't Be Effective When The Pain Becomes Worse | This concern is without any scientific or medical basis. Opioids can be used with good effect for as long as they are needed, and the dose can be adjusted to whatever level is needed for pain relief. The best way to manage pain is to control it early. |
| Fear of Tolerance | For many patients, their opioid dose remains stable over long periods of time. ⁸¹⁻⁸⁴ |
| Fear People Will Think You Are 'Giving Up' | Patients with pain that is well controlled are more likely to be able to manage other aspects of their illness and enjoy a better quality of life. Pain is also easier to control if it is treated promptly, so it is important that pain is treated as soon as possible. |
| Opioids Hasten Death | Studies show that good pain management using opioids has actually improved not only quality but also length of life. ⁸⁴⁻⁸⁸ |
| Fear About Personal Limitations. | For non-commercial driving in Canada, taking opioids does not mean that you can no longer drive. The decision about whether it is safe to drive is left to the individual. If the dose of opioid has been stable and drowsiness is not a problem, then driving is allowed; if there is drowsiness from the medications, if your dose is being titrated upward due to increased pain, then it is not safe to drive. |

Pasero Opioid-Induced Sedation Scale (POSS)⁷⁸

| | |
|----------|---|
| S | sleep, easy to arouse |
| 1 | awake and alert |
| 2 | slightly drowsy, easily aroused |
| 3 | frequently drowsy, arousable, drifts off to sleep during conversation |
| 4 | somnolent, minimal or no response to physical stimulation |

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DEFINITION

Fatigue or “**asthenia**”^{1,2} is a subjective symptom, ranging from tiredness to exhaustion, that is out of proportion to recent activity.³⁻⁵ It occurs as a result of disease, emotional state and/or treatment, and may be acute or chronic. Major features⁵ include: easy tiring and reduced capacity for activity; generalized weakness; and impaired concentration, with memory loss and emotional lability.

PREVALENCE

Fatigue is the most frequent and debilitating symptom in advanced cancer (60-90%)⁵ and advanced chronic illness (75-99%).⁶⁻⁸

IMPACT

Fatigue is expected in disease progression and is part of the normal clinical changes that occur approaching end of life.⁶ It interferes with function and impacts all aspects of well-being and quality of life, leading to economic consequences and significant distress for both patient and family.^{6, 7, 9-13}

Education and anticipatory guidance is essential to support patient and family self-management with coping abilities and to enable them to set realistic goals and expectations.⁸

STANDARD OF CARE

Step 1 | Goals of care conversation

Determine goals of care in conversation with the patient, family and interdisciplinary team. Refer to additional resources ([Additional resources for management of fatigue](#)) for tools to guide conversations and required documentation. Goals of care may change over time and need to be reconsidered at times of transition, e.g., disease progression or transfer to another care setting.

Step 2 | Assessment

Fatigue Assessment: Using Mnemonic O, P, Q, R, S, T, U and V⁶⁰

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| Mnemonic Letter | Assessment Questions <i>Whenever possible, ask the patient directly. Involve family as appropriate and desired by the patient.</i> |
|-------------------------------|---|
| O nset | When did you start to feel fatigued? How long does it last? How often does it occur? |
| P rovoking /Palliating | What brings it on? What makes it better? What makes it worse? |
| Q uality | What does it feel like? Can you describe it? |
| R egion/Radiation | Not applicable |
| S everity | How severe is this symptom? What would you rate it on a scale of 0-10 (0 being none and 10 being the worst possible)? Right now? At worst? On average? How bothered are you by this symptom? |
| T reatment | What medications and treatments are you currently using? Are you using any non-prescription treatments, herbal remedies, or traditional healing practices? How effective are these? Do you have any side effects from the medications and treatments? What have you tried in the past? Do you have concerns about side effects or cost of treatments? |
| U nderstanding | What do you believe is causing this symptom? How is it affecting you and/or your family? What is most concerning to you? How is this affecting your emotional, spiritual and social health? Have you had to change any of your daily activities? Does it impact your ability to work? Enjoy hobbies? Exercise? Visit with family and friends? Are there any other symptom(s) that accompany this symptom (e.g., shortness of breath)? |
| V alues | What overall goals do we need to keep in mind as we manage this symptom? What is your acceptable level for this symptom (0-10)? Are there any beliefs, views or feelings about this symptom that are important to you and your family? |

Symptom Assessment: Physical assessment as appropriate for symptom

A comprehensive history with careful systems review including sleep and psychiatric history, detailed physical examination, and review of prescribed and over the counter medication use, to identify side-effects and possible drug-drug interactions that may be reversible is of importance.² Identified underlying conditions and contributing factors should be assessed for reversibility and optimized, as appropriate, recognizing patient condition, preferences and goals of care.⁸

Diagnostics: consider goals of care before ordering diagnostic testing

- Diagnostic tests may include hemoglobin, WBC, serum sodium, potassium, calcium, magnesium, blood glucose, serum urea, creatinine, liver enzymes, triiodothyronine, thyroxine, drug levels (phenytoin, digoxin),^{49, 50} and urinalysis, as UTI can be common cause in frail patients.

Step 3 | Determine possible causes and reverse as possible if in keeping with goals of care (For more details, see [Underlying causes of fatigue in palliative care](#))

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Fatigue usually has multiple causes^{10,49-56} and may be related to underlying disease, treatments, or a variety of reversible and non-reversible factors. Symptom problems, psychosocial factors and mood disturbances, such as depression and anxiety,^{57,58} may all disrupt sleep and/or contribute to fatigue.

PRINCIPLES OF MANAGEMENT



When considering a management approach, always balance burden of a possible intervention against the likely benefit (e.g., does the intervention require transfer to another care setting?)

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- Focus on identifying and optimizing underlying conditions and somatic causes^{1, 2, 14}
- For mild fatigue (1-3/10), provide patient and family education on methods of energy conservation, and counselling to support self-management and coping. Encourage moderate physical activity to preserve muscle function.¹⁰
- For moderate fatigue (4-6/10), refer to Physiotherapy and Occupational Therapy to support comfort & safety in activities. Include pharmacological, and non-pharmacological approaches, as appropriate.
- For severe fatigue (7-10/10), provide counselling and anticipatory guidance to support coping and realistic expectations.
- Multidisciplinary team involvement is beneficial to support psychosocial, emotional and spiritual concerns.^{6, 8, 11}
- For patients who are near end of life, re-direct focus from physical function to other enjoyable activities. Eg. Massage, music
- Encourage the patient and family to prioritize meaningful activities, and to give themselves permission to take a less active role in housework, etc.

Step 4 | Interventions

LEGEND FOR USE OF BULLETS

Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence, using a modified GRADE process.

| | |
|--|--|
|  | Use with confidence: recommendations are supported by moderate to high levels of empirical evidence. |
|  | Use if benefits outweigh potential harm: recommendations are supported by clinical practice experience, anecdotal, observational or case study evidence providing low level empirical evidence. |
|  | Use with caution: Evidence for recommendations is conflicting or insufficient, requiring further study |
|  | Not recommended: high level empirical evidence of no benefit or potential harm |

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Non-pharmacological Interventions

Interventions available in the home and residential care facilities

-  **Physical activity or exercise** - Maintains independence, physical function, well-being, self-esteem and energy, in patients who are able.^{5, 6, 32-34} Moderate benefit for cancer-related fatigue.
-  **Moderate activity** helps maintain strength, performance and well-being in advanced cancer patients, but no change to fatigue.^{5, 36}
 -  limited evidence in palliative care patients.^{5, 33, 35} Tailor activity to patient status.
-  **Patient education and cognitive behavioural therapy** improves sleep and fatigue in patients with advanced-stage cancer; helpful for patients and families.^{5, 6, 37}
-  **Cognitive restructuring** to change dysfunctional beliefs, such as catastrophizing or feeling helpless with respect to fatigue.⁴¹⁻⁴³
-  **Multidisciplinary team involvement** supports psychosocial, emotional, spiritual and cultural concerns.^{6, 11}
-  **Physiotherapy** improves physical wellbeing, fatigue, depression, and overall quality of life, functional mobility, anxiety, stress, and depression.^{36, 38-40} Helps with de-conditioning⁵ in earlier stages. Passive range of motion exercises maintain flexibility and reduce painful tendon retraction in the immobile patients.⁵
-  **Occupational therapy** provides education/physical review to simplify tasks and conserve energy; recommends equipment to support safe transfers, mobility and self-care; and prevents further muscle atrophy, tendon retraction, and pressure ulcers.⁵

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Alternative and complementary therapy

-  Mind-body techniques, music and art therapy, and spiritual practices.
-  Massage has a beneficial effect on patient's experience of fatigue.⁶

Interventions requiring additional equipment or admission to acute care

-  **Transfusion of packed red blood cells** benefits severe anemia (hemoglobin <8g/dL). Improves patient fatigue, dyspnea and well-being for 15 days.^{5, 6} Consider patient status, goals and preferences. Short term benefit but risk of harm increases with multiple transfusions.
-  **Acupuncture** - benefits cancer-related fatigue and quality of life.^{5, 44}
-  Little evidence for acupuncture effect on fatigue in the palliative, chronic disease population.

Not recommended

-  **Parenteral Hydration.**⁴⁵ Benefit for fatigue uncertain, safety is not assured and may necessitate transfer from desired location.

Pharmacological interventions

Corticosteroids

-  Monitor closely for drug interactions and adverse effects. Dose varies with indication. Short term use of dexamethasone.¹⁵ Most commonly used at 2-4mg/d.⁵⁹
-  Methylprednisolone, 16 mg twice daily for one week; although very rarely used PO, also significantly improved fatigue.¹⁶
-  Limit duration of treatment for fatigue. No benefit shown beyond 7 to 15 days. Adverse effects increase with longer treatment^{16, 17} and higher doses. Give earlier in day to reduce insomnia. Physicians believe to be effective, but evidence is inconsistent.^{15, 17, 18}

Methylphenidate

-  Consider use if fatigue due to **opioids** or **depression**.¹⁹ Although lack of evidence, an individual trial could be appropriate, with monitoring for response and adverse effects.²⁰
-  Start with 5 mg daily (2.5 mg for elderly), increasing to twice daily: morning and at noon. Second dose given no later than 14:00 to minimize night-time insomnia. A favourable response occurs within one to a few days.²¹⁻²³ If no response, discontinue.
-  Adverse effects of agitation, restlessness, tachycardia, delirium, confusion and insomnia; limit dose patient tolerability and willingness to continue use.²⁴
-  Intolerable adverse effects occurred within 7 days in one-third of cancer patients, most on 5 mg daily.²² Note: Relative contraindication: pre-existing arrhythmia (e.g., AFib).

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Modafinil

 Benefit shown in cancer-related fatigue, but **ONLY** for those with severe fatigue $\geq 7/10$ on the Brief Fatigue Inventory (BFI).^{25, 26} Minimal toxicities shown.²⁶

 Not recommend use for mild or moderate fatigue.

Melatonin

 No benefit in palliative patients with advanced cancer, 20 mg/day²⁷

 Advanced breast cancer patients showed potential for improving circadian disruption resulting in improved sleep, quality of life, and fatigue, on 5 mg nightly²⁸

Not recommended

 **Erythropoiesis stimulating agents**²⁹⁻³¹ due to serious increased health risks and high cost.

Patient and family education

Education and counselling empowers patients and their family/caregivers to cope more effectively with fatigue^{1,5,10} and supports their ability to develop realistic expectations.⁸

-  Provide information on symptoms and expected disease progression to reduce feelings of anxiety and guilt related to patient's fatigue.
-  Encourage exercise as appropriate to capability.
-  Instruct on fatigue self-care through energy conservation and activity management.
-  Balance activity and rest: too much rest may increase fatigue. Exercise as able.
-  Request medication/dose changes in those that may be causing loss of energy.
-  Prepare patient and family to anticipate increasing need for activity assistance.
-  Encourage use of energy restoration strategies. This includes relaxation and pursuit of patient preferred enjoyable activities, e.g., music, massage, etc.
-  Direct focus away from fatiguing physical functions and towards other enjoyable activities.⁶ This helps transition understanding and acceptance.
-  Provide supportive, goal-tailored information about the dying process.

ADDITIONAL RESOURCES FOR MANAGEMENT OF FATIGUE

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Resources specific to Fatigue

- BC Guidelines: Fatigue and weakness
→ http://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/palliative2_fatigue.pdf
- BC's Heart Failure Network: Fatigue
→ <http://www.bcheartfailure.ca/wp-content/uploads/downloads/2015/01/Fatigue-Jan-2015.pdf>

General Resources

- **Provincial Palliative Care Line** – for **physician** advice or support, call **1 877 711-5757** In ongoing partnership with the Doctors of BC, the toll-free Provincial Palliative Care Consultation Phone Line is staffed by Vancouver Home Hospice Palliative Care physicians 24 hours per day, 7 days per week to assist physicians in B.C. with advice about symptom management, psychosocial issues, or difficult end-of-life decision making.
- BC Centre for Palliative Care: Serious Illness Conversation Guide
→ <http://www.bc-cpc.ca/cpc/>
- BC Guidelines: Palliative Care for the Patient with Incurable Cancer or Advanced Disease
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care>
- BC Palliative Care Benefits: Information for prescribers
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program>
- National Centre for Complementary and Alternative Medicine (NCCAM) for additional information on the use of non-pharmacological interventions
→ <https://nccih.nih.gov/>
- Canadian Association of Psychosocial Oncology: Pan-Canadian Practice Guideline: Screening, Assessment and Management of Psychosocial Distress, Depression and Anxiety in Adults with Cancer
→ http://www.capo.ca/wp-content/uploads/2015/11/FINAL_Distress_Guideline1.pdf
- Fraser Health psychosocial care guideline
→ <https://www.fraserhealth.ca/media/psychosocial%20care.pdf>

Resources specific to health organization/region

- Fraser Health
→ <http://www.fraserhealth.ca/health-professionals/professional-resources/hospice-palliative-care/>
- First Nations Health Authority
→ <http://www.fnha.ca/>

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- Interior Health
→ <https://www.interiorhealth.ca/YourCare/PalliativeCare/Pages/default.aspx>
- Island Health
→ http://www.viha.ca/pal_eol/
- Northern Health
→ <https://www.northernhealth.ca/Professionals/PalliativeCareEndofLifeCare.aspx>
- Providence Health
→ <http://hpc.providencehealthcare.org/>
- Vancouver Coastal Health
→ <http://www.vch.ca/your-care/home-community-care/care-options/hospice-palliative-care>

Resources specific to patient population

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians
→ <https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf>
- ALS Society of British Columbia 1-800-708-3228
→ www.alsbc.ca
- BC Cancer Agency: Symptom management guidelines
→ <http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management>
- BC Renal Agency: Conservative care pathway and symptom management
→ <http://www.bcrenalagency.ca/health-professionals/clinical-resources/palliative-care>
- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management
→ <http://www.bcheartfailure.ca/for-bc-healthcare-providers/end-of-life-tools/>
- Canuck Place Children's Hospice
→ <https://www.canuckplace.org/resources/for-health-professionals/>
 - 24 hr line – 1.877.882.2288
 - Page a Pediatric Palliative care physician – 1-604-875-2161 (request palliative physician on call)
- Together for short lives: Basic symptom control in pediatric palliative care
→ http://www.togetherforshortlives.org.uk/professionals/resources/2434_basic_symptom_control_in_paediatric_palliative_care_free_download

UNDERLYING CAUSES OF FATIGUE IN PALLIATIVE CARE^{1, 2, 10, 14}

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- Advanced aging-Frailty
- Anemia
- Anorexia - cachexia
- Autonomic dysfunction
- Bleeding
- Cancer: tumor, host-derived factors, cytokines
- Cardiac disease (CHF)
- Central nervous system (CNS) abnormalities
- Deconditioning (bed rest/immobility)
- Dementia (end-stage)
- Dehydration
- Endocrine disorders
- Electrolyte imbalances (hypercalcemia, hyponatremia, etc)
- Gastro-intestinal symptoms (nausea, vomiting, diarrhea, constipation)
- HIV-AIDS (end-stage)
- Hypoxemia
- Infection
- Other symptoms (dyspnea, pain, drowsiness, depression)
- Over-exertion
- Liver Failure (end-stage)
- Medications – monitor regularly
- Metabolic disorders
- Muscle abnormalities
- Neuro-muscular Diseases (ALS, MS)
- Nutritional deficiencies
- Para-neoplastic neurological syndromes
- Psychological issues
- Renal Failure (end-stage)
- Respiratory disease (copd, ild)
- Side-effects of Treatment
- Sleep disorders (insomnia)
- Unrelieved symptoms (pain, dyspnea, N/V, delirium, etc)

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Medication details for fatigue are included in the body of the guideline

Prices for prescription drugs may be obtained from BC PharmaCare. The British Columbia Palliative Care Benefits Plan <http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/palliative-formulary.pdf> provides province wide drug coverage for many of the recommended medications—check website to confirm coverage. **Consider price when choosing similarly beneficial medications, especially when the patient / family is covering the cost.**

FATIGUE MANAGEMENT ALGORITHM

No management algorithm included in this document.

FATIGUE EXTRA RESOURCES OR ASSESSMENT TOOLS

Brief Fatigue Inventory

- <https://www.mdanderson.org/research/departments-labs-institutes/departments-divisions/symptom-research/symptom-assessment-tools/brief-fatigue-inventory.html>
- <http://www.rehabmeasures.org/Lists/RehabMeasures/DispForm.aspx?ID=1190>

Edmonton Symptom Assessment System-revised (ESASr)⁴⁶

- <http://palliative.org/NewPC/professionals/tools/esas.html>
- http://palliative.org/NewPC/_pdfs/tools/ESAS-r.pdf

European Cooperative Oncology Group Criteria (ECOG) Performance Status

- <http://ecog-acrin.org/resources/ecog-performance-status>

Functional Assessment of Chronic Illness Tool-Fatigue (FACIT-F)^{47,48}

- <http://qol.thoracic.org/sections/instruments/fj/pages/fact-f.html>
- <http://www.facit.org/FACITOrg/Questionnaires>

Palliative Performance Scale (PPSv2)

- http://www.victoriahospice.org/sites/default/files/pps_english.pdf

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DEFINITION

Pruritus or itch is defined as an intense cutaneous discomfort occurring with pathological change in the skin and mucous membranes which elicits vigorous scratching. It is a complex symptom with poorly characterized pathophysiology and is variable in its perceived quality and intensity.¹ It may be idiopathic or prodrome of disease.²

PREVALENCE

Pruritus is rare but troublesome, ranging from 1% at onset of administration of opioids to 25-85% for persons with advanced renal failure. Prevalence increases with age.^{2,3}

IMPACT

Can create significant suffering and morbidity leading to sleep deprivation, depression, anxiety, impaired quality of life, and even suicidal ideation.¹

STANDARD OF CARE

Step 1 | **Goals of care conversation**

Determine goals of care in conversation with the patient, family and interdisciplinary team. Refer to additional resources ([Additional resources for management of pruritus](#)) for tools to guide conversations and required documentation. Goals of care may change over time and need to be reconsidered at times of transition, e.g., disease progression or transfer to another care setting.

Step 2 | Assessment

Pruritus Assessment: Using Mnemonic O, P, Q, R, S, T, U and V³¹

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| Mnemonic Letter | Assessment Questions <i>Whenever possible, ask the patient directly. Involve family as appropriate and desired by the patient.</i> |
|-------------------------------|--|
| O nset | When did it begin? How long does it last? How often does it occur? |
| P rovoking /Palliating | What brings it on? What makes it better? What makes it worse? |
| Q uality | What does it feel like? Can you describe it? |
| R egion/Radiation | Where do you feel itchy? Is it in one area or your entire body? |
| S everity | Pruritus cannot be measured directly and is difficult to quantify. ^{4,5} Focus questions on impact on quality of life. May try questions using a rating scale: How severe is this symptom? What would you rate it on a scale of 0-10 (0 being none and 10 being the worst possible)? Right now? At worst? On average? How bothered are you by this symptom? Are there any other symptom(s) that accompany this symptom? (Existing itch measurement tools are too detailed and resource intensive for use in palliative care setting. ⁵) |
| T reatment | What medications and treatments are you currently using? Are you using any non-prescription treatments, herbal remedies, or traditional healing practices? How effective are these? Do you have any side effects from the medications and treatments? What have you tried in the past? Do you have concerns about side effects or cost of treatments? |
| U nderstanding | What do you believe is causing this symptom? How is it affecting you and/or your family? What is most concerning to you? |
| V alues | What overall goals do we need to keep in mind as we manage this symptom? What is your acceptable level for this symptom (0-10)? Are there any beliefs, views or feelings about this symptom that are important to you and your family? |

Symptom Assessment: Physical assessment as appropriate for symptom

Diagnostics: consider goals of care before ordering diagnostic testing.

Step 3 | Determine possible causes and reverse as possible if in keeping with goals of care

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- Pruritus should not be considered simply a skin disorder, but rather a systemic problem for which there are multiple causes. It is difficult to isolate these entirely and some degree of overlap is likely.⁶
- **Systemic etiology** may be present in 4-40% of all cases.⁶ Anxiety or fear may be both cause and consequence of pruritus.⁶
- Although it is normal to experience occasional mild or moderate pruritus, the **severe pruritus** seen in patients with advanced disease is usually associated with uremia (chronic renal failure), cholestasis, opioids, and hematologic disorders; it is a frequent complication of cholestasis.⁷ Solid tumours can cause pruritus via biliary obstruction (e.g., in pancreatic cancer). Dry skin also accompanies many of these conditions.⁸
- **Opioid-induced itch** is due to release of histamines and is more common with spinal opioids than with systemic opioids.⁸ May require switching of opioids.³¹

PRINCIPLES OF MANAGEMENT



When considering a management approach, always balance burden of a possible intervention against the likely benefit (e.g., does the intervention require transfer to another care setting?)

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- There is no universally effective treatment for palliative care patients due to different pathomechanisms.^{3,9}
- Combinations of systemic and topical agents often provide the best relief.¹
- Treatment evidence is stronger for systemic drug therapy than for topical therapy; however, topicals have fewer adverse effects.
- Treatment responses are very individual and cannot easily be predicted.¹⁰
- Medications inducing photosensitivity may exacerbate itching; these include: NSAIDs, diuretics, antineoplastics, ciprofloxin.¹¹
- Address other associated cluster symptoms associated with pruritus including sleep, depression and pain.
- A multi-disciplinary team approach is often essential.^{12,13} Difficult cases require consultation with other medical specialists, e.g., palliative physician and dermatologist.

Step 4 | Interventions

LEGEND FOR USE OF BULLETS

Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence, using a modified GRADE process.

| | |
|--|--|
|  | Use with confidence: recommendations are supported by moderate to high levels of empirical evidence. |
|  | Use if benefits outweigh potential harm: recommendations are supported by clinical practice experience, anecdotal, observational or case study evidence providing low level empirical evidence. |
|  | Use with caution: Evidence for recommendations is conflicting or insufficient, requiring further study |
|  | Not recommended: high level empirical evidence of no benefit or potential harm |

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Non-pharmacological interventions

Interventions available in the home and residential care facilities

-  **Tepid baths** with mild, unscented soap can be soothing and temporarily relieve the itch.^{1,8}
-  Add **baking soda** to late evening bath to form protective layer and maintain hydration.^{4,7}
-  **Dry skin** by **gently** patting with soft towel or use hair dryer on low setting.⁷
-  **Use a “soak and seal” method:** pat skin dry, lubricate the skin with a fragrance-free, cream-base emollient containing camphor or menthol (see **pharmacological interventions below**).
-  **Keep** finger and toe nails **short and filed**.
-  Provide **cotton gloves** for day or night use for those with strong urge to scratch.
-  **Apply tap water wet dressings** (e.g., cotton long underwear soaked in water) to the affected areas several times daily for 1–2 hours for excoriations and crusting due to scratching; provides temporary relief and hastens healing of injured skin.¹
-  **Loose, cotton clothing** is less irritating, minimizes heat retention and sweating.¹
-  **Avoid fragrant** topical agents, perfumes, perfumed soaps.⁸
-  **Cool packs** and loose, light cotton bedding.
-  Provide **cool humidified environment**.²

Non-pharmacological interventions continued on [next page](#)

Non-pharmacological interventions *continued*

Interventions requiring additional equipment or admission to acute care

-  **Ultraviolet B light therapy** performed 3 X a week may be useful in pruritus secondary to uremia, cholestasis and malignant skin infiltrations; may not be suitable for terminally ill persons.⁸ **Stent placement** helps pruritus from cholestasis secondary to pancreatic cancer (to decompress biliary obstruction)^{7,8,14} and might negate the need for any pharmacologic treatment, eliminating potential adverse side effects of certain drugs.⁸
-  **Endoscopic or percutaneous biliary tree decompression** should be considered in biliary obstruction.¹⁵

Pharmacological interventions (For more detailed pharmacological information, see [Medications for management of pruritus](#))

High quality evidence for interventions in palliative care patients is lacking; the diverse nature and presentation of pruritus hamper studies and drug selection.^{7,9}

-  **Antihistamines** are generally not helpful, as the role of histamine remains unclear.^{7,8,16}
 -  Antihistamines value maybe limited to relief via sedation and use at bedtime.^{4,9}
 -  Cetirizine is a very minimally sedating daytime antihistamine.
-  **Cholestyramine** is the only drug with a Canadian licensed indication for treatment of pruritus, for use associated with partial biliary obstruction.¹⁷
-  **Paroxetine's** effectiveness is cautiously assumed for general palliative pruritus treatment, yet its harm assessment is limited.^{3,9}
-  Sertraline at low daily doses can be effective; does not require dose adjustment in renal impairment. Adverse effects may be minimal.

Topicals

-  Mild to moderate potency corticosteroids (for inflammation), topical anesthetics (lidocaine, prilocaine, pramoxine), doxepin.²
-  Cooling products such as menthol (0.25-2%), camphor (1-3%) are used within emollient compounds.²
-  Ketamine (0.5-5%) with amitriptyline (1-2%) in compounded creams.^{18,19}
-  Avoid topical antihistamine creams due to risk of allergic contact dermatitis.^{7,20}

Other

-  Systemic corticosteroids have also been used for cholestatic pruritus.²¹
-  Case reports therapies have included: lidocaine infusion,²² ranitidine,²³ and indomethacin for pruritus in HIV patients.³

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-  Prevent boredom or anxiety in creative, personalized ways.⁷
-  Avoid vasodilators such as coffee, alcohol, spices and hot water.
-  Teach recommended non-pharmacologic strategies.

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Resources specific to Pruritus

- BC Cancer Agency symptom management guidelines for radiation dermatitis
→ <http://www.bccancer.bc.ca/nursing-site/Documents/16.%20Radiation%20Dermatitis.pdf>
- BC Cancer Agency symptom management guideline for acneiform rash
→ <http://www.bccancer.bc.ca/nursing-site/Documents/1.%20Acneiform%20Rash.pdf>
- BC Renal Agency pruritic treatment algorithm in hemodialysis patients
→ <http://www.bcrenalagency.ca/resource-gallery/Documents/SymptomManagementProtocolPruritus1.pdf>
- ESAS Renal
→ http://palliative.org/NewPC/_pdfs/tools/ESASr%20Renal.pdf

General Resources

- **Provincial Palliative Care Line** – for **physician** advice or support, call **1 877 711-5757** In ongoing partnership with the Doctors of BC, the toll-free Provincial Palliative Care Consultation Phone Line is staffed by Vancouver Home Hospice Palliative Care physicians 24 hours per day, 7 days per week to assist physicians in B.C. with advice about symptom management, psychosocial issues, or difficult end-of-life decision making.
- BC Centre for Palliative Care: Serious Illness Conversation Guide
→ <http://www.bc-cpc.ca/cpc/>
- BC Guidelines: Palliative Care for the Patient with Incurable Cancer or Advanced Disease
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care>
- BC Palliative Care Benefits: Information for prescribers
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program>
- National Centre for Complementary and Alternative Medicine (NCCAM) for additional information on the use of non-pharmacological interventions
→ <https://nccih.nih.gov/>
- Canadian Association of Psychosocial Oncology: Pan-Canadian Practice Guideline: Screening, Assessment and Management of Psychosocial Distress, Depression and Anxiety in Adults with Cancer
→ http://www.capo.ca/wp-content/uploads/2015/11/FINAL_Distress_Guideline1.pdf
- Fraser Health psychosocial care guideline
→ <https://www.fraserhealth.ca/media/psychosocial%20care.pdf>

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Resources specific to health organization/region

- Fraser Health
→ <http://www.fraserhealth.ca/health-professionals/professional-resources/hospice-palliative-care/>
- First Nations Health Authority
→ <http://www.fnha.ca/>
- Interior Health
→ <https://www.interiorhealth.ca/YourCare/PalliativeCare/Pages/default.aspx>
- Island Health
→ http://www.viha.ca/pal_eol/
- Northern Health
→ <https://www.northernhealth.ca/Professionals/PalliativeCareEndofLifeCare.aspx>
- Providence Health
→ <http://hpc.providencehealthcare.org/>
- Vancouver Coastal Health
→ <http://www.vch.ca/your-care/home-community-care/care-options/hospice-palliative-care>

Resources specific to patient population

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians
→ <https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf>
- ALS Society of British Columbia 1-800-708-3228
→ www.alsbc.ca
- BC Cancer Agency: Symptom management guidelines
→ <http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management>
- BC Renal Agency: Conservative care pathway and symptom management
→ <http://www.bcrenalagency.ca/health-professionals/clinical-resources/palliative-care>
- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management
→ <http://www.bcheartfailure.ca/for-bc-healthcare-providers/end-of-life-tools/>

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- Canuck Place Children’s Hospice
 - <https://www.canuckplace.org/resources/for-health-professionals/>
 - 24 hr line – 1.877.882.2288
 - Page a Pediatric Palliative care physician – 1-604-875-2161 (request palliative physician on call)
- Together for short lives: Basic symptom control in pediatric palliative care
 - http://www.togetherforshortlives.org.uk/professionals/resources/2434_basic_symptom_control_in_paediatric_palliative_care_free_download

UNDERLYING CAUSES OF PRURITUS IN PALLIATIVE CARE

Information is contained in the body of the document.

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| Drug, Action | Indication(s) | Dose, therapeutic range | Adverse Effects, Precautions, Dosing Concerns |
|---|---|---|--|
| Cholestyramine (resin binds intestinal biliary acids, interrupts enterohepatic cycle of biliary acids) ^{2, 7, 24} | Cholestasis, Solid tumors and paraneoplastic disorders, Uremia | Initial: 4 g PO taken 30 minutes before breakfast and 30 minutes after breakfast. As needed, add 2 doses at lunchtime (before and after the meal) or at dinnertime (before and after the meal) Maximum: 16 to 32 g/day. | Nausea, constipation, abdominal discomfort, flatulence, unpleasant taste. Often poorly tolerated. Breakfast dosing time effective as pruritogens are stored in the gallbladder overnight. MANY drug interactions, commonly requires dose spacing. Take one hour before or 4-6 hours after other medication to avoid absorption impairment. |
| Doxepin (H1, H2, muscarinic antagonist) ² | Cholestasis, Psychogenic | Initial: 10 to 25 mg PO HS Increase by 25 mg/day. Maximum: 75 to 300 mg per day in divided doses. | Drowsiness, xerostomia Powerful H1 effect (more than hydroxyzine or diphenhydramine). QTc prolongation if dose over 100 mg per day. |
| Gabapentin (blocks central nociceptive transmissions to brain) ^{4,15,16} | Lymphoma, Opioid-induced, Uremia, if failure of other treatments | Initial: 100 mg PO TID. Hemodialysis patients: 100 to 300 mg PO once after HD Pre-op: 1200 mg single dose Maximum: up to 1200 mg/day. | Drowsiness, dizziness, fatigue, ataxia, peripheral edema, visual disturbances, unsteadiness. Adjust dose for reduced renal function. In extended therapy, (optimally) reduce dose over a minimum of one week. Very few drug interactions |

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| Methylnaltrexone (mu opioid receptor antagonist) ^{25, 26} | Cholestasis | Initial: 12 mg SC daily Repeat dosing every 1 to 2 days PRN. | Abdominal pain (SC 21-29%), flatulence (13%), nausea (9-12%). Contraindicated in known or suspected GI obstruction or if an increased risk of recurrent obstruction. Costly. Acts peripherally; did not reverse opioid analgesia in two patients. |
| Mirtazapine (H1,5-HT2, 5HT3 receptor antagonist) ^{2,26} | Cholestasis, Lymphoma, Solid tumors and paraneoplastic disorders, uremia if failure of other treatments | Initial: 7.5 to 15 mg PO HS. If partial relief after one week, increase by 15 mg. Maximum: 30 mg/day. | Drowsiness, but may be beneficial for itch suffering at HS. Weight gain. No anxiety or nausea at start of use (unlike SSRI's). Few drug interactions. Use caution if history of seizures. Discontinuation symptoms have been reported upon abrupt withdrawal; reduce dose gradually if possible. Therapeutic effect may disappear after 4 to 6 weeks. Clearance is reduced in moderate and severe renal function. Administer with caution in hepatic impairment. |
| Naloxone (mu opioid receptor antagonist) ^{2, 27} | Cholestasis, Opioid-induced, Psychogenic | Initial: 0.2 mcg per kg per minute IV infusion. Double the infusion rate every 3 to 4 hours PRN Maximum: 0.8 mcg/kg/min. | Withdrawal syndrome: if on opioids (reversing analgesia), or if high endogenous opioids (e.g., in cholestasis, liver damage or uremia). May change to PO naltrexone after 24 to 48 hours of use. |

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| Naltrexone (mu opioid receptor antagonist) ^{2,3,24,26} | Cholestasis, Psychogenic, Uremia | Initial: 6.25 to 12.5 mg PO daily. Increase by increments of 12.5 to 25 mg BID or TID. Maximum: 300 mg/day. | Vertigo (19-50%) is a major fall risk concern. Dizziness, nausea (29%), abdominal pain, diarrhea, appetite loss, vomiting, arthralgia, anxiety. Withdrawal syndrome; if on opioids (reversing analgesia), or if high endogenous opioids (e.g., in cholestasis, liver damage or uremia) Hepatotoxicity at high doses. |
| Ondansetron (5-HTs antagonist) ^{1-3, 6, 24} | Cholestasis, Opioid-induced, Psychogenic, Uremia | Initial: 4 mg PO, SC, IV once or twice daily. Maximum: 8 mg TID. | Headache (17%), constipation (11%), diarrhea (16%), xerostomia (5%), increased liver enzymes (17%), fever. Benefit may be ineffective or dose dependent. Single 4 mg IV may be effective for 4 hours; 8 mg IV effective for 16 hours. Costly. |

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| Paroxetine (serotonin reduced via 5-HT ₃ receptor reduction) ^{2,8,26,28} | Cholestasis, Solid tumors and paraneoplastic disorders, Opioid induced, if failure of other treatments | Initial: 5 to 10 mg PO daily. Increase by 10 mg per day, every 4 to 5 days. Maximum: 20 mg/day. | Nausea and vomiting, especially first 3 days. Drowsiness. Lower or less frequent dosing may be needed in severe renal impairment (CrCl less than 30 mL/min). Lower and less frequent dosing may be necessary in patients with severe hepatic impairment. Use caution in seizure disorder patients. Pruritus may return within 3 days if discontinued. Avoid abrupt discontinuation as may increase risk of serious discontinuation symptoms; gradual dose reduction and monitoring recommended. Antipruritic effect may disappear after 2-3 months for some patients |
| Rifampin (also called Rifampicin, e.g., in Europe) (inhibits biliary acid reuptake, interrupts enterohepatic cycle of biliary acids) ^{2,26} | Cholestasis | Initial: 75 mg PO daily. Double dose every week PRN. Maximum: 300 mg BID. | MANY drug interactions; assess risk prior to initiation. Monitor liver function, particularly in first 2 months of treatment. Do not drink alcohol while taking. Take 1 hour before or 2 hours after a meal with a full glass of water. To avoid long term adverse effects, (hepatitis, hemolytic anemia, renal failure, thrombocytopenia) stop if pruritus completely resolves. |

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|--|---------------|--|---|
| Sertraline (serotonin reduced via 5-HT ₃ receptor reduction) ^{2,26,29,30} | Cholestasis | Initial: 25 mg PO daily. Adjust by 25 mg per day every 4 to 5 days. Maximum: 100 mg/day. | Adverse effects: insomnia, nausea. Duration of antipruritic effect sustained throughout full treatment use, unlike paroxetine. Use caution in seizure disorder patients. No adjustment needed in renal impairment. |

† Off-label. PO = by mouth IV = Intravenous, SC = Subcutaneous, TID = three times daily, QID = four times daily ODT = oral dissolving tablet CSCI = continuous subcutaneous infusion.

Prices for prescription drugs may be obtained from BC PharmaCare. The British Columbia Palliative Care Benefits Plan <http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/palliative-formulary.pdf> provides province wide drug coverage for many of the recommended medications— check website to confirm coverage. **Consider price when choosing similarly beneficial medications, especially when the patient / family is covering the cost.**

PRURITUS MANAGEMENT ALGORITHM

No management algorithm included in this document.

PRURITUS EXTRA RESOURCES OR ASSESSMENT TOOLS

No extra resources or assessment tools included in this document.

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DEFINITION

Bleeding is the loss of blood or blood escaping from the circulatory system. Associated symptoms depend on the duration and rate of bleeding.¹ The terms **‘massive’ or ‘catastrophic’ are sometimes preferred over the term ‘terminal’ hemorrhage** because not all large bleeds result in death.² This guideline will refer to **severe bleeding** which is a large amount of blood loss. The clinical presentation of bleeding in the palliative care setting is variable. It may be visible or invisible; volumes may vary from low-grade oozing to massive and catastrophic, continuous or intermittent. It may be localized or from multiple sites.² **Exsanguination** is defined as the blood loss of >150 mL per minute or loss of entire blood volume in 24 hours.^{3,4}

PREVALENCE

Massive hemorrhage has been estimated to affect less than 2% of patients in the palliative care setting.³ In cancer patients, the nature of the bleeding depends on type of primary cancer and location of the metastases with tumour erosion of aorta, pulmonary, carotid and femoral arteries being the greatest likelihood.^{3,5,6} Bleeding also occurs in terminally ill patients with non-cancer diagnoses, e.g., variceal hemorrhage occurs in 25-35% of patients with cirrhosis.²

IMPACT

Catastrophic, massive bleeding warrants special attention because of its dramatic and traumatic clinical presentation and the profound distress it causes to patients, families and caregivers.² While a catastrophic bleed is not painful for the patient, it is often described as a terrifying experience for the patient, the family and staff.^{7,8} This affects not only the family’s experience at the time of death but runs the risk of affecting the nature of their grief and bereavement.

STANDARD OF CARE

Step 1 | Goals of care conversation

Determine goals of care in conversation with the patient, family and inter-disciplinary team. Refer to additional resources ([Additional resources for management of severe bleeding](#)) for tools to guide conversations and required documentation. Goals of care may change over time and need to be reconsidered at times of transition, e.g., disease progression or transfer to another care setting.

Step 2 | Assessment

Severe bleeding Assessment: Using Mnemonic O, P, Q, R, S, T, U and V³²

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| Mnemonic Letter | Assessment Questions <i>Whenever possible, ask the patient directly. Involve family as appropriate and desired by the patient.</i> |
|-------------------------------|--|
| O nset | Has herald or sentinel bleeding occurred, i.e., have you had any bleeding or oozing at this point? When did it begin? How long does it last? How often does it occur? |
| P rovoking /Palliating | Is there any action/movement that provokes bleeding? Is there anything that makes it worse? Or better? |
| Q uality | If there is bleeding, how would you describe it? Is it gradual and slow? Does it ooze, gush or spurt? |
| R egion/Radiation | Where is the bleeding located? Is there more than one site of bleeding? |
| S everity | How severe is this symptom? What would you rate it on a scale of 0-10 (0 being none and 10 being the worst possible)? Right now? At worst? On average? How bothered are you by this symptom? Are there any other symptom(s) that accompany this symptom (e.g., pain, dyspnea, anxiety)? Approximately how much blood is lost in 24 hours (depending on site ask about soaked bed linen, number of saturated gauzes, color of water in the toilet)? |
| T reatment | What medications and treatments are you currently using? Are you using any non-prescription treatments, herbal remedies, or traditional healing practices? How effective are these? Do you have any side effects from the medications and treatments? What have you tried in the past? Do you have concerns about side effects or cost of treatments? Have any special dressings been used to absorb bleeding? |
| U nderstanding | What do you believe is causing this symptom? How is it affecting you and/or your family? What is most concerning to you? |
| V alues | What overall goals do we need to keep in mind as we manage this symptom? What is your acceptable level for this symptom (0-10)? Are there any beliefs, views or feelings about this symptom that are important to you and your family? |

Symptom Assessment: Physical assessment as appropriate for symptom

A comprehensive history and physical examination is required to determine the risk of a severe bleed, potential origins and the potential for multiple sites. Massive bleeding may take place in the lung without the presence of hemoptysis so listening to lung sounds is very important.⁹ Initial bleeding in the form of hemoptysis or bleeding from a malignant neck wound may signal an impending severe bleed.

Diagnostics: consider goals of care before ordering diagnostic testing

Step 3 | Determine possible causes and reverse as possible if in keeping with goals of care (For more details, see [Underlying causes of severe bleeding in palliative care](#))

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Bleeding causes can be classified within six categories

(1) cancer invasion and destruction, (2) treatment-related causes, (3) thrombocytopenia/marrow failure, (4) nutritional deficits, (5) drugs, and (6) coagulation disturbances.² See [Underlying causes of severe bleeding in palliative care](#) for further specific primary causes.

PRINCIPLES OF MANAGEMENT



When considering a management approach, always balance burden of a possible intervention against the likely benefit (e.g., does the intervention require transfer to another care setting?).

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- Assess risks and need for anticipatory management
 - Develop an anticipatory care plan (see [Severe bleeding extra resources or assessment tools](#) for more detail) where possible and appropriate
 - Make sure all professionals and services involved are aware of the care plan, including out-of-hours services.⁷
- Manage bleed event
 - Keep calm, be present, comfort, reposition, shield visual trauma with dark towels, summon help, be supportive with help of medications and warm blankets. See further details in section 5 and 6.
- Post bleed management¹⁰
 - Offer de-briefing to family and health care team. This is critical
 - Provide ongoing support as necessary for relatives and staff members.
 - Dispose of clinical waste appropriately.

Step 4 | Interventions

LEGEND FOR USE OF BULLETS

Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence, using a modified GRADE process.

| | |
|--|--|
|  | Use with confidence: recommendations are supported by moderate to high levels of empirical evidence. |
|  | Use if benefits outweigh potential harm: recommendations are supported by clinical practice experience, anecdotal, observational or case study evidence providing low level empirical evidence. |
|  | Use with caution: Evidence for recommendations is conflicting or insufficient, requiring further study |
|  | Not recommended: high level empirical evidence of no benefit or potential harm |

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Non-pharmacological interventions^{2, 4, 6, 8, 10, 12-14:}

Interventions available in the home and residential care facilities

It may be possible to manage a severe bleed in the home or residential care facility with appropriate planning and support for the patient, family and staff; all of these interventions do not necessarily require additional equipment or admission to acute care.

| ABCD Response | |
|--------------------------|--|
| A - Assure | Assure patient this event has been anticipated. Reassure that you will stay with them throughout. |
| B - Be Present | Stay with patient. Considered the most important intervention. Ensure that someone is with the patient at all times. |
| C - Calm, Comfort | Employ intensive calmness. Comfort: verbally soothe, hold, touch or hug them. |
| D - Dignity | Maintain patient dignity. Minimize visual impact. Cover patient with dark towels or sheets. Use basins, sheets or absorptive dressings with an impermeable backing. Clean patient face with moist cloths often. |

Non-pharmacological interventions continued on [next page](#)

Non-pharmacological interventions continued

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| Management of the Bleed | |
|-------------------------|---|
| REPOSITION | <p>Adjust body position for blood flow, comfort, minimize sighting of blood:</p> <p>Use recovery position to keep airway clear.</p> <p>For hematemesis - place in left lateral decubitus position.</p> <p>For hemoptysis - position onto the side in which the presumed bleeding lung is in the dependent position, e.g., place a patient whose right lung is bleeding on their right side.</p> |
| SUMMON HELP | Call for help. |
| APPLY PRESSURE | Assess individual circumstances; use direct pressure cautiously with friable tissue. Local pressure may be appropriate for an external wound. |
| MEDICATIONS | Midazolam use when required; see below and Medications for management of severe bleeding . |
| WARMTH | Warm blankets can offset hypothermia from rapid bleed. |
| SUPPORT | Goals of care, plan a debrief for all who were present. |
| NOTIFY | Inform family, physician, others. |

Pharmacological Interventions

(see [Medications for management of severe bleeding](#) for Medication table)

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-  Use sedation as quickly as possible to relieve distress, when practical and timely.^{13, 14}
-  **Midazolam 10 mg dose is most commonly used for major bleeds.**^{2, 10, 12-17}
 -  Give midazolam IV (preferred) bolus, if IV access is possible.^{6, 10}
 -  Alternatively give SC, IM (large deltoid or gluteal muscle), or buccal.^{7, 12, 14, 18}
 -  Repeat dose if needed. IV within 5 minutes, SC, IM, buccal within 5 to 15 minutes.¹³
-  Alternatives include: Lorazepam 4 mg IV/SC/sublingual¹⁰ and Ketamine 150 to 250 mg IV, or 500 mg IM (large deltoid or gluteal muscle).^{13, 16}
-  Opioids are indicated for pain or dyspnea.¹⁴ Hemorrhage is usually not painful.^{6, 13, 16}

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-  Ask if they want to know about risks, potential developments; ask if they are willing to participate in anticipatory planning for a potential bleed event.
 -  As appropriate, involve patient and family in the plan creation.
 -  As appropriate, share the supportive anticipatory care plan.
 -  Reassure that in the event of a bleed, the person WILL be kept comfortable and will not be left alone; unconsciousness could occur quickly.³
 -  Remind patient and family that not all anticipated bleeds materialize.
-  Anticipatory plan should
 -  Provide awareness and supportive information, and enhance patient/ family coping.
 -  Include a NO CPR order and/or NO CPR advance directive.
 -  Teach calm approach and value of comforting presence to patient.
 -  Identify who to call; unprepared caregivers may panic, calling emergency services that are required to institute resuscitative measures. Include after hours nurse phone line if available in your region.
 -  Ensure family and caregivers understand intent of medication is solely to relieve distress and anxiety, not to hasten death.¹¹
 -  Inform that if anti-anxiety drugs help, they will need time to prepare and work, which could be too slow if bleed is large or very rapid.
 -  Consider the implications of asking a caregiver and family member to administer prefilled syringes of sedatives in the event of a massive bleed if they are alone when it begins.²

See [Severe bleeding extra resources or assessment tools](#) for further specifics about anticipatory planning.

ADDITIONAL RESOURCES FOR MANAGEMENT OF SEVERE BLEEDING

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Resources specific to Severe Bleeding: No additional resources specific to severe bleeding included in this document

General Resources

- **Provincial Palliative Care Line** – for **physician** advice or support, call **1 877 711-5757** In ongoing partnership with the Doctors of BC, the toll-free Provincial Palliative Care Consultation Phone Line is staffed by Vancouver Home Hospice Palliative Care physicians 24 hours per day, 7 days per week to assist physicians in B.C. with advice about symptom management, psychosocial issues, or difficult end-of-life decision making.
- BC Centre for Palliative Care: Serious Illness Conversation Guide
→ <http://www.bc-cpc.ca/cpc/>
- BC Guidelines: Palliative Care for the Patient with Incurable Cancer or Advanced Disease
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care>
- BC Palliative Care Benefits: Information for prescribers
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program>
- National Centre for Complementary and Alternative Medicine (NCCAM) for additional information on the use of non-pharmacological interventions
→ <https://nccih.nih.gov/>
- Canadian Association of Psychosocial Oncology: Pan-Canadian Practice Guideline: Screening, Assessment and Management of Psychosocial Distress, Depression and Anxiety in Adults with Cancer
→ http://www.capo.ca/wp-content/uploads/2015/11/FINAL_Distress_Guideline1.pdf
- Fraser Health psychosocial care guideline
→ <https://www.fraserhealth.ca/media/psychosocial%20care.pdf>

Resources specific to health organization/region

- Fraser Health
→ <http://www.fraserhealth.ca/health-professionals/professional-resources/hospice-palliative-care/>
- First Nations Health Authority
→ <http://www.fnha.ca/>
- Interior Health
→ <https://www.interiorhealth.ca/YourCare/PalliativeCare/Pages/default.aspx>
- Island Health
→ http://www.viha.ca/pal_eol/

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- Northern Health
→ <https://www.northernhealth.ca/Professionals/PalliativeCareEndofLifeCare.aspx>
- Providence Health
→ <http://hpc.providencehealthcare.org/>
- Vancouver Coastal Health
→ <http://www.vch.ca/your-care/home-community-care/care-options/hospice-palliative-care>

Resources specific to patient population

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians
→ <https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf>
- ALS Society of British Columbia 1-800-708-3228
→ www.alsbc.ca
- BC Cancer Agency: Symptom management guidelines
→ <http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management>
- BC Renal Agency: Conservative care pathway and symptom management
→ <http://www.bcrenalagency.ca/health-professionals/clinical-resources/palliative-care>
- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management
→ <http://www.bcheartfailure.ca/for-bc-healthcare-providers/end-of-life-tools/>
- Canuck Place Children's Hospice
→ <https://www.canuckplace.org/resources/for-health-professionals/>
 - 24 hr line – 1.877.882.2288
 - Page a Pediatric Palliative care physician – 1-604-875-2161 (request palliative physician on call)
- Together for short lives: Basic symptom control in pediatric palliative care
→ http://www.togetherforshortlives.org.uk/professionals/resources/2434_basic_symptom_control_in_paediatric_palliative_care_free_download

UNDERLYING CAUSES OF SEVERE BLEEDING IN PALLIATIVE CARE^{2,6}

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| 1. Overall risk factors for bleeding in cancer patients | |
|---|--|
| Thrombocytopenia < 20,000/uL | Myelodysplasia |
| Large head and neck cancers | Severe liver disease and metastatic liver disease |
| Large centrally located lung cancers | High-dose radiation therapy |
| Refractory chronic and acute leukemias | Oral anticoagulants |
| Risk factors for severe hemorrhaging in head and neck cancers | |
| Radical neck dissection | Fungating tumours with arterial invasion |
| High-dose radiotherapy | Sentinel bleed |
| Postop healing problems | Direct observation during surgery or imaging (e.g. magnetic resonance imaging) of artery wall invasion |
| Visible arterial pulsation | |
| 2. Drug Causes <i>Using references^{2, 6}</i> | |
| Drugs - Drug Classes | Specific Causative Examples* |
| Anticoagulants, Antiplatelet drugs | ASA, Apixiban 0.1-2.1% (major), Clopidogrel 0.8-3.7% (major), Dabigatran 0.3-3.3%, Dalteparin up to 13.6% (major), Danaparoid up to 45%, Dipyridamole, Enoxaparin up to 4% (major), Heparin, Rivaroxaban 17.4-28.3% (treatment of deep vein thrombosis or pulmonary embolism), Ticagrelor 1.7-3.9% (major), Ticlopidine %, Tinzaparin 0.8% (major), Warfarin |
| Antidepressants | Citalopram, Desvenlafaxine, Doxepin, Duloxetine, Escitalopram, Fluoxetine, Fluvoxamine, Paroxetine, Sertraline <0.1%, Venlafaxine |
| Antiretrovirals | Indinavir 2.7-39%, Ritonavir 2.7-46%, Saquinavir 2.7-14% |
| Chemotherapy | Bevacizumab 40 % (glioblastoma any grade), Capecitabine, Cyclophosphamide, Gemcitabine 9-17%, Hydroxyurea, Ifosfamide, Imatinib 1-53% (chronic myeloid leuk-emia [CML] all grades), Irinotecan 1-5%, Nilotinib 1.1-1.8% (CML), Paclitaxel 10-14%, Sorafenib 15.3% (renal cell carcinoma [RCC]), 17.4% (thyroid carcinoma), Sunitinib 37% (RCC), 18% (GI stromal tumor) 22% (pancreatic neuroendocrine tumors), Thiotepa 28% (IV high dose) |
| Corticosteroids | Dexamethasone 2.5% (gastrointestinal), Prednisone |
| Non-Steroidal Anti-inflammatory Agents | Celecoxib, Diclofenac, Ibuprofen 4-10%, Indomethacin, Ketorolac, Meloxicam, Naproxen |
| Other | Dexmedetomidine 3%, Everolimus 3% (renal cell carcin-oma), Meropenem 1.2%, Sodium Valproate 1-27% (throm-bocytopenia), Sotalol 2%, Testosterone, Topiramate 4.4% |

* There are many medications that are reported to cause bleeding, thrombocytopenia. If no specific percentage incidence shown for each drug, the known occurrence rate not reported.⁶

¹⁰ This table above provides some examples. Consult pharmacist if additional assistance is required.

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| Drug (classification) | Dose, Therapeutic Range | Onset, Adverse Effects, Precautions and Dosing Concerns |
|--|--|--|
| Midazolam*† (benzodiazepine) | <u>Stat dose:</u> 10 mg IV, SC, IM, buccal <u>Repeat dose</u> 5 min IV 5 to 15 min SC, IM, buccal | <p>Onset: 1 to 5 min IV,²⁰ 5 to 10 min SC,²¹ 5 to 15 min IM into deltoid muscle^{10, 18}</p> <p>Adverse effects: IV administration over 2 to 3 minutes suggested to minimize hypotensive effects, reported in up to 30% of patients.^{22, 23} However, consider immediacy of bolus administration within clinical context.</p> <p>Contraindicated if hypersensitivity to benzodiazepines.</p> <p>Precautions in patients with prior paradoxical reaction history to benzodiazepines. Prior or concurrent opioid dosing may increase respiratory depressant effects.</p> <p>Dosing: Review dose, 10 mg commonly recommended.^{2, 10, 12-17}</p> <p>A single dose in an emergency situation, must be sufficiently adequate for a rapid and predictable effect.¹³ Lower doses, such as 2.5 to 5 mg may be appropriate if bleeding is brisk but not rapidly fatal.^{2, 13}</p> <p>Weight based dosing of 0.2 mg/Kg dose IV or SC suggested for urgent palliative bleed sedation (where known).⁴</p> <p>Higher doses may be needed; if already on background benzodiazepines, heavy alcohol or substance use.^{7, 10, 14}</p> <p>Effectiveness of route of administration: Peripheral circulation shutdown during hypovolemic shock has some experts suggesting that bioavailability will be especially compromised for IM and SC administration.^{2, 10, 16} SC route may be unpredictable.¹⁰ Most references continue to suggest SC use.^{2, 4, 14, 17} For buccal administration, place dose between the patient's cheek and gum.¹⁴</p> <p>Storage of prefilled syringes: 5 mg/mL undiluted reported stable for 36 days at 25° C when protected from light.²⁴</p> <p>Sterility assurance beyond 24 hours of preparation unknown, assess importance, duration of storage within clinical context.</p> <p>Recently, Health Canada has cautioned regarding storage of medications in disposable plastic syringes citing risk of potency concerns.²⁵ Replacement every 4 to 7 days has been suggested.^{15, 26}</p> |

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| Drug (classification) | Dose, Therapeutic Range | Onset, Adverse Effects, Precautions and Dosing Concerns |
|--|--|---|
| Lorazepam*† (benzodiazepine) | 4 mg x 1 dose IV, SL, SC, IM or buccal | Onset: 5 minutes SL. ^{21, 27} May be as long as 20-30 minutes. ²⁸ IV onset faster than SC or SL. ²⁹ Sublingual onset similar to IM, SC. ^{28, 29} For buccal administration: in patients with a dry mouth, the tablet should be dissolved in a few drops of warm water, or drop SL tablet into a syringe, add water to dissolve, then place dose between the patient's cheek and gum. ^{27 30} |
| Ketamine*† (anesthetic) | 150 to 250 mg IV x 1 dose 500 IM x 1 dose ^{13, 16} | Onset: 1 minute IV, ³¹ 5 min IM. ²¹ Adverse effects include paradoxical excitation. IM injection volume large, requiring multiple sites of injection. |

* Dose effect for massive bleed treatment not studied, is expert opinion only.

†Off-label. PO = by mouth IV = Intravenous, SC = Subcutaneous, TID = three times daily, QID = four times daily ODT = oral dissolving tablet CSCI = continuous subcutaneous infusion.

Prices for prescription drugs may be obtained from BC PharmaCare. The British Columbia Palliative Care Benefits Plan <http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/palliative-formulary.pdf> provides province wide drug coverage for many of the recommended medications— check website to confirm coverage. **Consider price when choosing similarly beneficial medications, especially when the patient / family is covering the cost.**

SEVERE BLEEDING MANAGEMENT ALGORITHM

No management algorithm included in this document.

SEVERE BLEEDING EXTRA RESOURCES OR ASSESSMENT TOOLS

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Anticipatory Planning Review List for Bleed Risk Patients^{2, 6, 10, 14, 16, 19}

Note: use the below checklist as a guide for creating a care plan

FOR ALL SETTINGS

Discussion

- The discussion should be consistent with the patient's information, needs and preferences; the care plan needs to be compatible with the patient's wishes.²
- All patients with a potential bleed need a plan of care created for use by family and health care providers.
- Additionally, some patients may wish to create a Bleeding Plan specific to their situation (e.g., in the event of a bleed, music to be played, dim lights in room, persons to phone or be present, sedation to be initiated or not).
- Store plans and Bleed Kit in accessible, convenient locations. Ensure appropriate awareness of these locations.

Contact Lists (individualized for this patient/family and this situation)

- 24 hr access in event of bleed at home, psychosocial counselling, other: Name, Telephone Number.

Supportive Resources

- The primary objective in managing a severe bleed is to minimize distress and potential trauma for the patient, family and staff.⁶
- Create a Bleed Kit: Ensure a supply of dark sheets or towels along with other equipment (gloves, aprons, plastic sheet, and clinical waste bags) in one organized container. Keep readily available.
- Explain the rationale for dark towels – to reduce the visible impact and decrease distress anxiety from seeing large volumes of blood.^{14, 19}
- Have several face cloths close to bedside to wipe patient's mouth, face.

Provide for Emergency On-Demand Medication Care Orders

- Orders written, or initiate pre-printed facility orders.
- Consider route, pre-insertion and management of parenteral access device.
- Medication and doses should reflect pre-existing conditions, benzodiazepine exposure. See [Medications for management of severe bleeding](#)
- Parameters: When to initiate, sedation target or need for use of sedation scales.
- Review suitability of prefilled syringe of medication to be on-hand, or use of locked storage cabinet.¹⁶
- Clarify if opioids have an emergency role, usually limited to that of pain or dyspnea.

Severe bleeding extra resources or assessment tools continued on [next page](#)

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Assess bleeding risk of Current Medications

- Anticoagulants, chemotherapy, corticosteroids, non-steroidal anti-inflammatory agents, selective serotonin receptor antagonists, sodium valproate. **See others in [Underlying causes of severe bleeding in palliative care](#).**
- Modify risk factors; stop unnecessary drugs; appropriately reduce/stop suspected drug causes; and consider a switch to drug option of lower bleed risk propensity.
- Assess benefits versus burden of continuing prophylactic anticoagulation treatments.
- Consider consultation with a pharmacist for drug-related risk management.
- Assess if specific preventative medication measures could have a role (e.g., proton pump inhibitors, tranexamic acid, topicals). Discuss further with palliative team consultants.

Team Planning, Communication

- Ensure there is multidisciplinary team involvement and documentation. Suitably share with other teams and involved care members.
- Confirm team understanding of action priorities. Acknowledge that crisis medications may have little role due to the speed of event, with a duration that last only minutes and insufficient time for therapeutic effect.^{2, 19}
- Ensure clarity that medication intent is to relieve patient distress, not to hasten death.^{2, 16}
- Reflect current care site in plans, and foresee if site transfers might occur.
- Provide staff education and awareness of patient's own management, goals of care.
- Plan for who will clean up after an event and how to contact them.¹⁰

Other Anticipatory Management

- Acknowledge that any major bleed should be managed the same way, regardless of knowing which will be a terminal event.¹⁶
- Assess suitability of continuous subcutaneous midazolam infusion for other indications, such that an on-demand bolus dose could be administered.
- Assess need for the addition of an opioid (e.g., if patient has pre-existing pain or dyspnea).

Severe bleeding extra resources or assessment tools continued on [next page](#)

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FOR HOME (COMMUNITY) SETTINGS

Discussion

- Ensure family (in home setting) have 24-hour contact number(s) and designate people who will be nearby for support.
- Confirm patient family acceptance and understanding that medications for distress are planned for and readily available should a severe bleed occur.
- Enquire if caregivers feel able to administer needed medication.
- Establish administration responsibility.
- Pre-plan at home for individual prescriptions or Palliative drug kits as appropriate.

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DEFINITION

Constipation is the difficult passage of stools, less frequent than normal for the individual.¹⁻³ It includes straining, a sensation of incomplete evacuation, and stool consistency that ranges from small, hard lumps to a large bulky mass. It may cause discomfort or pain.^{2, 4-6, 8} **Diarrhea** is the passage of 3 or more loose stools a day, with urgency. Careful clarification is required to determine diagnosis since reports of diarrhea may include: as a single loose stool, frequent small stools, fecal incontinence, or liquid bypassing due to impaction.⁹⁻¹³

PREVALENCE

Constipation is a significant problem in the palliative care population^{14, 15} affecting 41% of non-cancer patients,¹⁶ 30-50% of patients with cancer,¹⁷⁻¹⁹ and 35-70%, and as high as 87-90%^{6,20} of patients using opioids.²¹⁻²⁷ It is more common in women and affects 24-50% of the elderly.²⁸⁻⁴⁰ Constipation increases as normal overall function decreases and burden of disease increases.⁴¹ **Diarrhea** is not common in palliative care, affecting less than 10% of cancer patients admitted to hospice or hospital.¹⁰

IMPACT

Constipation causes significant suffering through physical symptoms such as abdominal distention, anorexia, nausea and vomiting, halitosis, abdominal and rectal pain, as well as psychological distress leading to headaches, agitation⁸⁰ and delirium.¹ Up to 1/3 of patients modify opioid use to avoid constipation.⁴²⁻⁴⁵ In older adults, constipation is associated with fecal impaction and/or fecal incontinence,⁴⁶ which may be mistaken as diarrhea. This is an embarrassing, distressing and exhausting symptom for both the patient and family, and impacts dignity, mood and relationships.^{6, 9, 10} Fecal impaction can also cause urinary retention,⁴⁷⁻⁴⁹ painful fissures, ulceration, bleeding and anemia.⁵

STANDARD OF CARE

Step 1 | Goals of care conversation

Determine goals of care in conversation with the patient, family and interdisciplinary team. Refer to additional resources ([Additional resources for management of constipation](#)) for tools to guide conversations and required documentation. Goals of care may change over time and need to be reconsidered at times of transition, e.g., disease progression or transfer to another care setting.

Step 2 | Assessment

Constipation Assessment: Using Mnemonic O, P, Q, R, S, T, U and V⁵⁰

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| Mnemonic Letter | Assessment Questions ^{1, 3, 6, 9, 10, 14, 15, 50, 51} <i>Whenever possible, ask the patient directly. Involve family as appropriate and desired by the patient.</i> |
|-------------------------------|---|
| O nset | When did it begin? How long does it last? How often does it occur? When was your last bowel movement? |
| P rovoking /Palliating | What brings it on? What makes it better? What makes it worse? What is your appetite like? How is your daily intake of food and fluids? How is your mobility? Do you need help to the bathroom/commode? When toileting? Do you have enough privacy? Do you have pain or any other problems? |
| Q uality | What is your normal bowel pattern? Are your bowel movements (BM) less frequent than usual? What do the stools look like? Are they smaller or harder than usual? Do you have discomfort or strain when passing stool? Is there controllable urge or sensation, prior to BM? Are you able to empty you bowels completely when desired? Do you have stool leakage or incontinence? |
| R egion/Radiation | Not applicable |
| S everity | How severe is this symptom? What would you rate it on a scale of 0-10 (0 being none and 10 being the worst possible)? Right now? At worst? On average? How bothered are you by this symptom? Are there any other symptom(s) that accompany this symptom? |
| T reatment | What medications and treatments are you currently using? Are you using any non-prescription treatments, herbal remedies, or traditional healing practices? How effective are these? Do you have any side effects from the medications and treatments? What have you tried in the past? Do you have concerns about side effects or cost of treatments? |
| U nderstanding | What do you believe is causing this symptom? How is it affecting you and/or your family? What is most concerning to you? Do you get any other symptoms: pain, nausea/vomiting, loss of appetite, bloating, gas, blood or mucous in stools, headaches or agitation? Do you have any urinary problems? Do you have any previous trauma which may impact how we manage your bowel movements (e.g., rectal interventions may re-traumatize people with past abuse)? How can we make sure you feel safe and respected? Are you worried about incontinence? |
| V alues | What overall goals do we need to keep in mind as we manage this symptom? What is your acceptable level for this symptom (0-10)? Are there any beliefs, views or feelings about this symptom that are important to you and your family? |

Step 2 | Assessment continued on [next page](#)

Symptom Assessment: Physical assessment as appropriate for symptom

Conduct a detailed history and physical examination, including a rectal or stomal exam.^{1, 10, 52-54} Review medications, medical/surgical conditions, psychosocial and physical environment.^{10, 50, 52} **Differentiate fecal impaction with liquid stool bypass from diarrhea.**¹⁰ Further investigations should be tailored to patient prognosis, goals of care, access to health-care resources, and the potential benefits of a precise diagnosis.¹⁴

Diagnostics: consider goals of care before ordering diagnostic testing

- Blood tests are rarely needed but, depending on clinical presentation, CBC, electrolytes, calcium and thyroid function should be evaluated.^{10, 55}
- If obstruction is suspected, X-ray to determine if partial or complete, high or low.^{10, 52, 56}

Step 3 | Determine possible causes and reverse as possible if in keeping with goals of care (For more details, see [Underlying causes of constipation in palliative care](#))

Constipation is often multifactorial in persons with advanced disease.^{10, 14, 46, 57} Predisposing risk factors are many (see [Underlying causes of constipation in palliative care](#)); most common include: older age, reduced intake, immobility, advanced disease, and use of anticholinergic and/or opioid medications.^{10, 57, 58} Opioids are a significant, but not exclusive, cause of constipation⁴¹; therefore, focus should be broader than this single cause.⁵⁷

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PRINCIPLES OF MANAGEMENT



When considering a management approach, always balance burden of a possible intervention against the likely benefit (e.g., does the intervention require transfer to another care setting?)

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- Prevention of constipation is key when risk factors exist (e.g., opioids, decreased intake, decreased physical activity).
- Increase and monitor fluids, dietary fibre, and physical activity, as tolerated.^{6, 10, 50}
- Identify and correct modifiable risk factors.^{6, 7, 10, 59}
- Discontinue fiber in debilitated patients if unable to maintain hydration, or when bowel obstruction is suspected.^{3, 52}
- Anticipate constipating effects of opioids and ensure a prophylactic laxative^{15, 60} unless bowel obstruction or diarrhea.^{1, 41, 55, 59-61}
- Oral measures are preferred and reduce need for rectal interventions.^{2, 10}
- Regularly monitor bowel pattern and patient satisfaction to adjust to desired effect.^{1, 7}
- Use practice tools to improve management: checklists, laxative protocols, audits.^{2, 3, 59, 62-64}
- Involve interdisciplinary team.⁵⁹ Consider personal, psychosocial and cultural perspectives.⁶
- Constipation is often progressively more challenging over time in end-of-life patients.

Step 4 | Interventions

LEGEND FOR USE OF BULLETS

Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence, using a modified GRADE process.

| | |
|--|--|
|  | Use with confidence: recommendations are supported by moderate to high levels of empirical evidence. |
|  | Use if benefits outweigh potential harm: recommendations are supported by clinical practice experience, anecdotal, observational or case study evidence providing low level empirical evidence. |
|  | Use with caution: Evidence for recommendations is conflicting or insufficient, requiring further study |
|  | Not recommended: high level empirical evidence of no benefit or potential harm |

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Interventions available in the home and residential care facilities

It may be possible to manage constipation in the home or residential care facility with appropriate planning and support for the patient, family and staff; all of these interventions do not necessarily require additional equipment or admission to acute care.

-  **Encourage** hydration, fibre intake and mobility, **as tolerated**^{3, 14, 52, 82}
-  **Wheat bran and prunes** improve bowel function,⁶⁴ as tolerated.
-  Refer to **physiotherapy and/or OT** for appropriate exercise and mobility supports¹⁰ as immobility may be more constipating than opioids.^{14, 59, 83}
-  **Biofeedback training** with physiotherapist may also benefit.⁶⁵
-  **Avoid use of bedpans.**^{14, 84} Ensure privacy, personal preference, promote independence and convenience during toileting.^{3, 52, 69, 85, 86}
-  There is little or no empirical evidence for other complementary approaches.¹⁰
-  Probiotics, have some evidence of benefit in constipation,⁸⁰ but may also harm.⁸⁷ Avoid use in severely ill or immunocompromised patients.⁸⁸

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ORAL LAXATIVES ARE FIRST-LINE THERAPY FOR CONSTIPATION

Recommended first-line oral laxatives: Sennosides, Lactulose, Polyethylene Glycol

-  Effectiveness of each appears similar based on expert opinion^{79, 89}; therefore, seek patient preferences.^{10, 15, 90, 91} Other factors impacting selection will include: cost, patient performance status, tolerance to effects, and ability to swallow.^{2, 3, 58} See [Medications for management of constipation](#) for more information about medications for management.
-  Opioid-induced constipation (OIC): the constipating effects of opioids are persistent. When opioids are started, **prophylactic laxatives are usually required**, and should be continued for the duration of opioid use.^{15, 60}
-  Sennosides may be the most useful single laxative when an opioid is prescribed.^{6, 10, 52, 63, 90, 92, 93}
-  A combination of a stimulant (e.g., sennosides), plus an osmotic laxative to moisturize and to soften stool (e.g., lactulose or polyethylene glycol (PEG)) may be required, particularly for opioid-induced constipation.^{2, 6, 15, 60, 62}
-  Use a stepwise approach, starting with simple, economical laxatives.¹⁴ See the [Constipation and bowel obstruction management algorithm](#).

Titration of Oral Laxatives

-  Titrate laxative doses **every 1 to 2 days** according to response.^{10, 15, 59}
-  Once current regimen satisfactory and well tolerated, continue with it, reviewing regularly with the patient; explain importance of preventing constipation.¹
-  As the dose of opioids increases, the dose of laxatives often needs to increase, with dosing twice daily (breakfast/bedtime) or even three times daily,^{6, 90} up to the maximum recommended or tolerable.^{15, 90, 94, 95}
-  The proportional dose of stimulant versus osmotic laxative is guided by stool consistency and tolerance.

If faecal leakage: reduce the dose of the osmotic laxative.^{2, 90} If colic (usually alongside hard stools): increase the osmotic laxative relative to the stimulant,² and/or divide the total stimulant daily dose into smaller, more frequent doses.⁶³
-  Evaluate patient tolerance and adverse effects from laxatives. **Refer to [Constipation and bowel obstruction management algorithm](#).**
-  Resolve diarrhea from laxatives by holding drugs for 1 to 2 days; restart at a lower dose.⁹⁶
-  Stop oral laxatives in the last few days of life when patients are no longer able to receive medication and their level of consciousness diminishes. Rectal care then is rare.^{2, 59, 96}

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Use of Rectal Measures: When Standard Oral Laxatives are Unsuccessful

Rectal Interventions (suppository, enema, manual extraction) should be used infrequently.⁶ See [Constipation and bowel obstruction management algorithm](#) and [Constipation and bowel obstructions extra resources or assessment tools](#) for further rectal measures information.

Refractory Constipation: When Standard Optimum Oral and Rectal Measures are Unsuccessful

-  Consult a palliative care specialist for refractory opioid-induced constipation or for specific, complex patient needs including spinal cord compression and cognitive impairment.^{2, 59}
-  When OIC suspected, and response to other standard measures is inadequate, opioid antagonists (e.g., methylnaltrexone, naloxegol) may be suitable with specialist advice.² Use only after failure of standard laxative therapy, to augment, not replace laxatives.⁶³ See [Constipation and bowel obstruction management algorithm](#) for more information.^{97, 98}

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-  Explain normal bowel function; this varies from person to person.⁶⁷
-  A daily bowel movement is not necessary. As long as stools are soft and easy to pass,^{68, 69} every 2 to 3 days is acceptable.^{70,71}
-  Don't ignore the urge to have a bowel movement. Try within 30 to 60 minutes following a meal, when the gastro colic reflex commonly occurs.^{11, 72-74}
-  Avoid excess straining as this may be harmful in some medical conditions.^{11, 64, 72}
-  Toilet in sitting position with use of a raised toilet seat, foot stool or bedside commode.
-  Privacy during toileting^{11, 13, 22, 72, 73, 75, 76} helps reduce anxiety/aids relaxation.
-  Advance pain control helps improve comfort and mobility.^{11, 64, 72}
-  Teach how to differentiate between oozing stool and diarrhea.

Teach constipation prevention

-  Increase fluids, dietary fibre, and mobility as tolerated; this is less possible over time.
-  Nutritional liquids, milkshakes, cream soups, fruit juices may aid appetite/activity.⁶⁷
-  A fruit laxative can be made with prunes, dates, figs and raisins.^{70, 72}
-  When oral intake and mobility are reduced, avoid extra fibre.^{3, 11, 13, 22, 73, 75, 77, 78} A laxative may be needed.
-  Patients on opioids for symptom control will need a stimulant laxative from the start of opioids to prevent ongoing constipating effects.^{10, 14, 25, 57, 79, 80} ([Medications for management of constipation](#))
-  Healthcare providers can help choose the laxative type most suited to individual needs.

Explain in advanced illness

-  Since the body continues to produce 1 to 2 ounces of stool per day, even if no oral intake,⁸¹ a laxative may still be needed. It can be stopped in the last days of life.

ADDITIONAL RESOURCES FOR MANAGEMENT OF CONSTIPATION

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Resources specific to constipation

- ALS of Canada fact sheet on constipation
→ <https://www.als.ca/wp-content/uploads/2017/04/ALSCAN-Constipation.pdf>
- BC Guidelines: Constipation
→ http://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/palliative2_constipation.pdf
- BC Cancer Agency: Constipation
→ <http://www.bccancer.bc.ca/nursing-site/Documents/3.%20Constipation.pdf>
- HealthLink BC: Managing Constipation in Adults with Diet
→ <https://www.healthlinkbc.ca/healthlinkbc-files/constipation-adults>
- BC Cancer Agency: Patient handout with suggestions for dealing with constipation
→ <http://www.bccancer.bc.ca/family-oncology-network-site/Documents/SuggestionsforDealingwithConstipation.pdf>

General Resources

- **Provincial Palliative Care Line** – for **physician** advice or support, call **1 877 711-5757** In ongoing partnership with the Doctors of BC, the toll-free Provincial Palliative Care Consultation Phone Line is staffed by Vancouver Home Hospice Palliative Care physicians 24 hours per day, 7 days per week to assist physicians in B.C. with advice about symptom management, psychosocial issues, or difficult end-of-life decision making.
- BC Centre for Palliative Care: Serious Illness Conversation Guide
→ <http://www.bc-cpc.ca/cpc/>
- BC Guidelines: Palliative Care for the Patient with Incurable Cancer or Advanced Disease
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care>
- BC Palliative Care Benefits: Information for prescribers
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program>
- National Centre for Complementary and Alternative Medicine (NCCAM) for additional information on the use of non-pharmacological interventions
→ <https://nccih.nih.gov/>
- Canadian Association of Psychosocial Oncology: Pan-Canadian Practice Guideline: Screening, Assessment and Management of Psychosocial Distress, Depression and Anxiety in Adults with Cancer
→ http://www.capo.ca/wp-content/uploads/2015/11/FINAL_Distress_Guideline1.pdf

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- Fraser Health psychosocial care guideline
→ <https://www.fraserhealth.ca/media/psychosocial%20care.pdf>

Resources specific to health organization/region

- Fraser Health
→ <http://www.fraserhealth.ca/health-professionals/professional-resources/hospice-palliative-care/>
- First Nations Health Authority
→ <http://www.fnha.ca/>
- Interior Health
→ <https://www.interiorhealth.ca/YourCare/PalliativeCare/Pages/default.aspx>
- Island Health
→ http://www.viha.ca/pal_eol/
- Northern Health
→ <https://www.northernhealth.ca/Professionals/PalliativeCareEndOfLifeCare.aspx>
- Providence Health
→ <http://hpc.providencehealthcare.org/>
- Vancouver Coastal Health
→ <http://www.vch.ca/your-care/home-community-care/care-options/hospice-palliative-care>

Resources specific to patient population

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians
→ <https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf>
- ALS Society of British Columbia 1-800-708-3228
→ www.alsbc.ca
- BC Cancer Agency: Symptom management guidelines
→ <http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management>
- BC Renal Agency: Conservative care pathway and symptom management
→ <http://www.bcrenalagency.ca/health-professionals/clinical-resources/palliative-care>
- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management
→ <http://www.bcheartfailure.ca/for-bc-healthcare-providers/end-of-life-tools/>

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- Canuck Place Children's Hospice
 - <https://www.canuckplace.org/resources/for-health-professionals/>
 - 24 hr line – 1.877.882.2288
 - Page a Pediatric Palliative care physician – 1-604-875-2161 (request palliative physician on call)
- Together for short lives: Basic symptom control in pediatric palliative care
 - http://www.togetherforshortlives.org.uk/professionals/resources/2434_basic_symptom_control_in_paediatric_palliative_care_free_download

UNDERLYING CAUSES OF CONSTIPATION IN PALLIATIVE CARE^{5, 6, 10, 11, 14, 39, 67, 77}

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| 1. Primary | |
|---------------------------------|--|
| • Advanced age | • Decreased intake |
| • Inactivity | • Low fiber diet |
| • Depression | • Poor fluid intake |
| • Sedation | • Physical or social impediments |
| 2. Secondary | |
| <i>Metabolic disturbances</i> | |
| • Dehydration | • Uremia |
| • Hyperglycemia | • Hypothyroidism |
| • Hypokalemia or Hypercalcemia | |
| <i>Concurrent Disease</i> | |
| • Diabetes | • Anal fissure |
| • Hernia | • Anterior mucosal prolapse |
| • Diverticular disease | • Hemorrhoids |
| • Colitis | • Spinal cord injury |
| • Rectocele | • Multiple Sclerosis, ALS |
| <i>Neurological disorders</i> | |
| • Cerebral tumors | • Sacral nerve infiltration |
| • Autonomic failure | • Spinal cord involvement/compression |
| <i>Structural abnormalities</i> | |
| • GI obstruction | • Radiation fibrosis |
| • Pelvic tumor mass | • Painful anorectal conditions (anal fissure, hemorrhoids, perianal abscess) |
| 3. Iatrogenic | |
| <i>Drugs - Drug Classes</i> | Specific Causative Examples |
| • 5HT3 Antagonists | • Ondansetron |
| • Antacids | • Aluminum, bismuth, calcium containing |
| • Anticholinergics | • Atropine, Glycopyrrolate, Hyoscine |
| • Anticonvulsants | • Gabapentin, Phenytoin |
| • Antidepressants | • Amitriptyline, Mirtazapine, Nortriptyline, Paroxetine, Sertraline |
| • Anti-diarrheal agents | • Loperamide, Kaolin/Pectin |
| • Antihypertensives | • Clonidine, Diltiazem, Nifedipine, Verapamil |
| • Antiparkinsonian agents | • Levodopa, Pramipexole, Selegiline |
| • Antipsychotics | • Haloperidol, Olanzapine, Quetiapine, Risperidone |
| • Chemotherapy | • Capecitabine, Temozolomide, Vincristine |
| • Diuretics | • Furosemide, Hydrochlorothiazide when result in dehydration |
| Gastrointestinal agents | Cholestyramine, Sodium Polystyrene Sulfonate |
| Hormonal agents | Octreotide |
| Opioids | All. Fentanyl, Methadone may be least constipating |
| Psyllium/Fiber | Occurs if insufficient fluid co-administered |
| Supplements | Iron or calcium |

There are many medications that are reported to cause constipation.⁹⁹ This table above provides some examples. Consult pharmacist if additional assistance is required.

MEDICATIONS FOR MANAGEMENT OF CONSTIPATION

Avoid laxatives, especially stimulants, if intestine is fully obstructed; seek consult.

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| Drug, Action | Dose, Therapeutic Range | Onset, Adverse Effects, Precautions and Dosing Concerns |
|---|--|--|
| Sennosides / Senna stimulant | <u>Starting dose:</u> 1 to 2 tablets PO at bedtime or 10 mL syrup. <u>Maximum daily tablet dose:</u> 36 mg PO TID ^{95,100} | 6 to 12 hours. ^{6,90} Intestinal colic is principal adverse effect ⁹² and may be similar to the cramping of severe constipation. Contraindicated in abdominal pain, nausea and vomiting, intestinal obstruction. ⁶⁹ Long term use considered safe. ^{10,14} Start at bedtime, if dose increases required, add next dosing time at breakfast. This timing best matches drug onset to natural gastrocolic peristalsis. Irritable bowel syndrome patients may experience painful cramps; osmotic laxatives are often preferred. ⁹⁵ |
| Lactulose osmotic | <u>Starting dose:</u> 15 mL PO daily with food. <u>Maximum daily dose:</u> 30 mL PO BID ^{55,101} | 1 to 2 days. ^{52,69} Abdominal bloating, flatulence (20% for the first few days), nausea (may be reduced if diluted or taken with meals), intestinal colic. ⁹⁰ Rarely causes serious electrolyte disorders or volume overload. ^{10,52,69} Contraindicated in galactosemia, intestinal obstruction. ⁶⁹ Avoid in lactose-intolerant patients. ⁵² Use with hot tea, hot water or juices to improve unpalatable sweet taste. ^{6,10} Lactulose does not affect diabetes mellitus management. ⁹⁰ Effectiveness requires a sufficiently high fluid intake. ¹ |
| Polyethylene Glycol "PEG" osmotic | <u>Starting dose:</u> 17 g PO daily. <u>Maximum daily dose:</u> ☐ 17 g PO BID ⁹⁰ to TID ⁶⁹ ☐ PCF5- BID, OB 139TID | 1 to 3 days. ⁶⁹ Nausea, bloating, occasional vomiting, stomach cramps. ⁶⁹ Requires 125 to 250 mL fluid intake daily per 17 g dose. ^{69,102} Contraindicated in intestinal obstruction or perforation, inflammatory bowel conditions (Crohn's disease, ulcerative colitis). ⁶⁹ Adverse effect profile may be better than other oral laxatives. ^{62,91} Use cautiously in patients unable to tolerate the fluid volume needed, e.g., if nauseated or frail. ¹ Used safely up to 6 to 12 months. ⁵¹ |
| Glycerin Suppositories osmotic, lubricant | Dose: 1 supp PR x 1 | 15 to 30 min. ^{1,90} Adverse effects rare but may include mild rectal irritation. ^{51,103} Avoid suppositories in patients with severely reduced white cell or platelet counts due the risk of bleeding or infection. ⁶ Suppositories should be retained for 15 minutes. ^{6,103,104} |
| Bisacodyl Suppositories stimulant | Dose: 1 supp PR x 1 | 20 to 60 min, up to 3 hours. ⁹⁰ Side effects rare but can cause occasional abdominal cramps and diarrhea or local rectal inflammation. ⁹⁰ Can worsen pre-existing rectal tears and anal fissures. ⁵⁵ Occasionally causes faecal leakage. Avoid suppositories in patients with severely reduced white cell or platelet counts due the risk of bleeding or infection. ⁶ Place suppository against rectal wall, not into faeces, to ensure effectiveness. ⁹⁰ |

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| Drug, Action | Dose, Therapeutic Range | Onset, Adverse Effects, Precautions and Dosing Concerns |
|--|--|--|
| Micro-enema osmotic, softener | <u>Starting dose:</u> 5 mL PR x 1 <u>Maximum dose:</u> 10 mL PR daily | 5 to 20 min, up to 60 min. ^{1, 90} Risk of intestinal necrosis: avoid use with sodium polystyrene sulfonate containing products. Do not use in the presence of abdominal pain, nausea, fever or vomiting. Contents include sodium citrate, sorbitol and sodium lauryl sulfoacetate ¹¹⁴ |
| Mineral Oil Enema (stool softener) | <u>Dose:</u> 130 mL PR x 1 <u>Maximum dose:</u> 1 enema PR daily | 2 to 15 minutes Warm to room temperature before use. ⁹⁰ |
| Sodium-phosphate enema osmotic | <u>Starting dose:</u> 130 mL PR x 1 <u>Maximum dose:</u> 1 enema PR daily | 2 to 5 minutes, up to 30 minutes. ^{1, 90} Elderly patients (over 65) are particularly at risk of serious electrolyte disturbances. ¹⁰⁵ Fatalities have been reported. ^{90, 105} Contraindicated in renal failure. ¹⁰⁰ Avoid multiple applications to minimize risk of adverse effects. ¹⁰³ If enemas are ever used regularly, must monitor for electrolyte, fluid imbalances, rectal trauma. ⁹⁶ Warm to room or body temperature before use. ^{1, 90} |
| Methylnaltrexone peripheral opioid receptor antagonist | Subcutaneous injection every 2 days as needed. Dose is weight based: 33-37 kg=6 mg 38-61 kg= 8 mg 62-114 kg=12 mg 115-126 kg=18 mg Outside these ranges, dose 0.15 mg/kg. Reduce doses by 50% when creatinine clearance is less than 30 mL/min. | 24 minutes to 4 hours. ^{106, 107} Abdominal pain, diarrhea, nausea, flatulence. Rare: flushing, delirium, severe diarrhea leading to dehydration and subsequent cardiovascular collapse, extrasystoles. ⁹⁸ Caution: Gastrointestinal (GI) perforation is a risk of this medication for patients with advanced illness such as: cancer, GI malignancy, GI ulcer, and Ogilvie's syndrome and taking medications such as bevacizumab, non-steroidal anti-inflammatory drugs and steroids. ¹¹⁵ To be used in conjunction with ongoing laxative therapy when laxatives alone are insufficient for treatment of opioid-induced constipation for advanced illness palliative care patients. ^{106, 107} Stop if response inadequate after four doses. ¹⁰⁷ No drug interactions with cytochrome P450 metabolized drugs. ¹⁰⁷ Balance drug cost alongside staffing costs, patient outcomes. ^{97, 98} |

Medications for management of constipation continued on [next page](#)

MEDICATIONS FOR MANAGEMENT OF CONSTIPATION

CONTINUED

| Definition | Drug, Action | Dose, Therapeutic Range | Onset, Adverse Effects, Precautions and Dosing Concerns | |
|------------------------------|---|--|--|--|
| Step 1 - Goals of care | Naloxegol peripheral opioid receptor antagonist | <u>Usual dose:</u> 12.5 to 25 mg PO daily | 6 to 12 hours. ¹⁰⁸ 50% of people respond within 12 hours. ¹⁰⁹ | |
| Step 2 - Assessment | | <u>Maximum daily dose:</u> 25 mg PO daily | Naloxegol is indicated for the treatment of opioid-induced constipation in adult patients with non-cancer pain who have had an inadequate response to laxatives. ¹⁰⁹ Usual starting dose is 25 mg daily. Reduce to 12.5 mg daily if moderate to end-stage renal impairment or if used concomitantly with weak CYP3A4 inhibitors (e.g., cimetidine, quinidine). Renal patients can increase dose to 25 mg daily if the 12.5 mg dose is well tolerated. ¹⁰⁹ Abdominal pain, flatulence, headache, diarrhea, and nausea ^{98, 109} | |
| Step 3 - Possible causes | | | | Anticipate numerous significant CYP3A4 drug interactions. |
| Principles of management | | | | Contraindicated in patients concomitantly receiving strong CYP3A4 inhibitors (e.g., ketoconazole, voriconazole, clarithromycin, protease inhibitors such as ritonavir). Interactions also occur with P-glycoprotein transporters (P-gp) modulators. ¹⁰⁹ Avoid grapefruit juice. ¹⁰⁹ |
| Step 4 - Interventions | | | | Contraindicated in known or suspected GI obstruction or patients at risk of recurrent obstruction due to potential for GI perforation. |
| Bullet legend | | | | Caution: if using in patients with any risk of impaired integrity of the gastrointestinal tract wall (e.g., severe peptic ulcer disease, Crohn's Disease, active or recurrent diverticulitis, infiltrative gastrointestinal tract malignancies or peritoneal metastases), consider the overall benefit/risk profile for a given patient. ¹⁰⁹ When started, all current laxative therapy should be stopped until clinical effect of naloxegol is determined. ¹⁰⁹ Does not cause systemic opioid withdrawal symptoms. Take in the morning on an empty stomach at least 1 hour prior to the first meal of the day or 2 hours post-meal. ¹⁰⁹ |
| Non-pharmacological | | | | Balance drug cost alongside staffing costs, patient outcomes. ^{97, 98} |
| Pharmacological | | | | |
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† Off-label. PO = by mouth IV = Intravenous, SC = Subcutaneous, TID = three times daily, QID = four times daily ODT = oral dissolving tablet, CSCI = continuous subcutaneous infusion.

Prices for prescription drugs may be obtained from BC PharmaCare. The British Columbia Palliative Care Benefits Plan (<http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/palliative-formulary.pdf>) provides province-wide drug coverage for many of the recommended medications; check website to confirm coverage. **Consider price when choosing similarly beneficial medications, especially when the patient/family is covering the cost.**

CONSTIPATION AND BOWEL MANAGEMENT ALGORITHM^{3,4,7}

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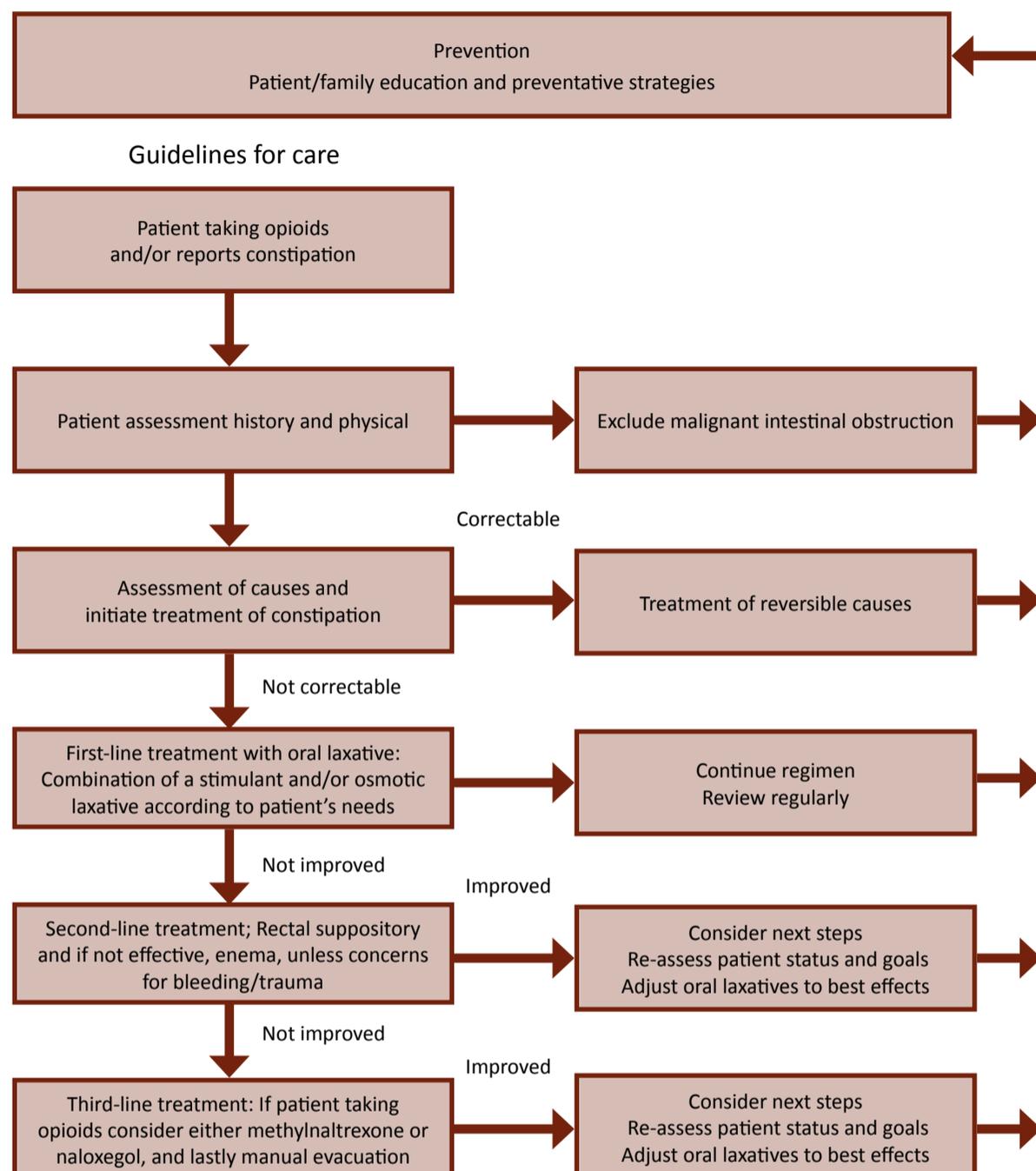
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Refer to [Medications for management of constipation](#) for further drug details including precautions and contraindications. Refer to guideline sections for specifics for prevention and patient/family education and preventative strategies

Algorithm adapted from Cancer Care Ontario – algorithm.⁷⁴

CONSTIPATION AND BOWEL OBSTRUCTIONS

EXTRA RESOURCES OR ASSESSMENT TOOLS

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- Victoria Bowel Performance Scale:¹¹⁰
 - <http://www.victoriahospice.org/sites/default/files/2bbbowelperformancescale.pdf>
- Bristol Stool Form Scale and Stool Diary:^{111, 112}
 - http://www.bowelcontrol.nih.gov/stool_diary_508.pdf

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DEFINITION

Nausea is the unpleasant subjective sensation of being about to vomit. It may occur in isolation or in conjunction with other gastrointestinal symptoms (e.g., vomiting)¹ and/or autonomic symptoms (e.g., pallor, cold sweat, salivation).²

Vomiting is the forceful expulsion of the gastric contents through the mouth or nose.²

PREVALENCE

Nausea and vomiting affects 40-60% of those receiving palliative care.²⁻⁵

IMPACT

Nausea and vomiting can be profoundly distressing for both patients and families, decreasing their quality of life.²⁻⁵ They may also delay active treatments such as chemotherapy.

STANDARD OF CARE

Step 1 | Goals of care conversation

Determine goals of care in conversation with the patient, family and interdisciplinary team. Refer to additional resources ([Additional resources for management of nausea and vomiting](#)) for tools to guide conversations and required documentation. Goals of care may change over time and need to be reconsidered at times of transition, e.g., disease progression or transfer to another care setting.

Step 2 | Assessment

Nausea and Vomiting Assessment: Using Mnemonic O, P, Q, R, S, T, U and V³²

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| Mnemonic Letter | Assessment Questions <i>Whenever possible, ask the patient directly. Involve family as appropriate and desired by the patient.</i> |
|-------------------------------|---|
| O nset | When did it begin? How long does it last? How often does it occur? |
| P rovoking /Palliating | What brings it on? What makes it better? What makes it worse? |
| Q uality | What does it feel like? Can you describe it? Do you vomit or just feel nauseated? Does it change when you change position? |
| R egion/Radiation | Not applicable |
| S everity | How severe is this symptom? What would you rate it on a scale of 0-10 (0 being none and 10 being the worst possible)? Right now? At worst? On average? How bothered are you by this symptom? Are there any other symptom(s) that accompany this symptom? |
| T reatment | What medications and treatments are you currently using? Are you using any non-prescription treatments, herbal remedies, or traditional healing practices? How effective are these? Do you have any side effects from the medications and treatments? What have you tried in the past? Do you have concerns about side effects or cost of treatments? |
| U nderstanding | What do you believe is causing this symptom? How is it affecting you and/or your family? What is most concerning to you? |
| V alues | What overall goals do we need to keep in mind as we manage this symptom? What is your acceptable level for this symptom (0-10)? Are there any beliefs, views or feelings about this symptom that are important to you and your family? |

Symptom Assessment: Physical assessment as appropriate for symptom

- Assess for signs of dehydration, jaundice, infection (e.g., fever) or drug toxicity.
- Neurological exam: assess for signs of a cranial lesion or raised intracranial pressure.
- Abdominal examination: assess for tenderness, organomegaly, ascites.
- +/- Rectal examination.

Step 2 | Assessment continued on [next page](#)

Step 2 | Assessment *continued*

Diagnostics: consider goals of care before ordering diagnostic testing

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Possible investigations are guided by the findings from the history and examination

- Blood work: CBC and differential, calcium, glucose, renal and liver function.
- Urine culture.
- Abdominal imaging: X-ray, ultrasound, CT/MRI.
- Endoscopy.

Step 3 | Determine possible causes and reverse as possible if in keeping with goals of care (For more details, see [Underlying causes of nausea and vomiting in palliative care](#))

Nausea and vomiting (NV) are separate but related symptoms present in many life-limiting conditions. Gastric stasis and chemical disturbance are the most common causes but the etiology is often multifactorial and may be difficult to establish.⁹

Underlying causes can be classified into 6 broad groups.^{2, 8, 9} (See [Underlying causes of nausea and vomiting in palliative care](#) for more detailed causes.)

- Chemical
- Cortical
- Cranial
- Vestibular
- Visceral or serosal
- Gastric Stasis (impaired gastric emptying)

PRINCIPLES OF MANAGEMENT



When considering a management approach, always balance burden of a possible intervention against the likely benefit (e.g., does the intervention require transfer to another care setting?)

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- Use cause determination, knowledge of emetogenic pathways, and a structured approach to guide antiemetic selection.^{10, 11}
- Use the first line drug recommended for the most likely cause of the symptom. **Refer to [Underlying causes of nausea and vomiting in palliative care](#) for drug selection and dosages.**
- A single antiemetic is sufficient in the majority of patients.¹³
- Monitor for symptom resolution and adverse effects for 48 hours. **Use [Management of nausea and vomiting titration algorithm](#) to guide further steps.**
- If symptoms persist, prescribe a regular antiemetic with different antiemetic to be given as needed.^{2, 8, 9, 14}

Step 4 | Interventions

LEGEND FOR USE OF BULLETS

Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence, using a modified GRADE process.

| | |
|--|--|
|  | Use with confidence: recommendations are supported by moderate to high levels of empirical evidence. |
|  | Use if benefits outweigh potential harm: recommendations are supported by clinical practice experience, anecdotal, observational or case study evidence providing low level empirical evidence. |
|  | Use with caution: Evidence for recommendations is conflicting or insufficient, requiring further study |
|  | Not recommended: high level empirical evidence of no benefit or potential harm |

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Non-pharmacological interventions

Non-pharmacological interventions provide their best relief for mild and moderate nausea and vomiting. In severe symptoms, their role is adjunctive to medications.

Interventions available in the home and residential care facilities

-  Meticulous attention to **oral care**; watch for signs of oral thrush. **Prevent constipation.**^{15, 16}
-  **Keep air and room fresh**; eliminate strong odors.¹⁷
-  **Increase oral intake** from ice chips, to clear fluids, to full fluids then to solid food as tolerated; Involve Clinical Dietician and/or other health disciplines as required.
-  **Aromatherapy:** peppermint or ginger oils reduce cancer related NV in small studies.²

Interventions requiring additional equipment or admission to acute care

-  Use of **acupuncture or acupressure** wrist bands.¹⁵
-  Offer **clinically assisted hydration** (IV or SC) if there is overall benefit or if functional status is high. Watch for fluid overload. Dying patients require lower volumes for hydration.⁹

Pharmacological interventions (refer to [Medications for management of nausea and vomiting](#), [Nausea and vomiting management algorithm](#) and [Nausea and vomiting extra resources or assessment tools](#) for more detailed information)

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Routes of Administration

-  Oral administration is preferred.^{2, 15} Rectal may be considered.
-  Parenteral medication (IV/SC) may be considered if the patient has vomiting, suspected malabsorption or gastric stasis.^{2, 15} After 3 days, consider converting to oral administration except in cases of mechanical intestinal obstruction.¹⁴
-  When switching routes of administration (such as oral to SC or IV) consider a bioavailability dosing adjustment. See [Nausea and vomiting management algorithm](#), and monitor response and adverse effects.

Low levels of distress (patient rating of 1 to 3/10)

-  Mild levels may respond to non-pharmacological actions.
-  Use the first-line drug for the most likely symptom cause. **Refer to [Underlying causes of nausea and vomiting in palliative care](#) for first, second and third line drug selection.**
-  Treat regularly for 48 hours, providing an additional PRN antiemetic drug.^{9, 10, 12}

Moderate level of distress (patient rating of 4 to 6/10)

-  Select the drug based on presumed etiology.
-  If cause is unknown (10-25% of patients)^{10, 18} or due to multiple factors (25-62%),^{3, 10, 18, 19} initial antiemetic choices are:
 - a) Metoclopramide: treats common causes of nausea, e.g., gastric stasis, partial bowel obstruction.⁹ **Avoid use in complete bowel obstruction.**
 - b) Haloperidol: treats chemical disturbances, another common cause of nausea.
 - c) Methotrimeprazine: a broad acting receptor antagonist.⁷

Severe distress (patient rating of 7 to 9/10)

-  Urgently assess cause and initiate appropriate drug treatment/interventions.
-  If inadequate control of severe nausea and vomiting within the first 48 hours, consider further management including:
 - a) Hospitalization, if required.
 - b) Consultation with palliative care physician.
 -  Further antiemetic titration drugs or options, including the combining of antiemetics which have a different or broader action, may be considered.

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Pharmacological interventions *continued*

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Refractory Nausea and Vomiting¹⁵

- ☰ May requires a consultation with a palliative care specialist.
- ☰ Prior to referral, professionals may wish to review if:
 - ☰ An appropriate antiemetic has been chosen, at optimal dose, and given by the appropriate route (often non-oral due to compromised oral absorption) for an adequate time period.¹⁵
 - ☰ Continued vomiting is an obstruction; duodenal/gastric outflow or high small bowel.¹⁵

Practice Points for Antiemetic Pharmacological Management

- ☰ Antiemetics tend to suppress vomiting more readily than nausea; an increase of the antiemetic dose may improve nausea control.¹⁸
- ☰ Haloperidol and methotrimeprazine have long elimination half-lives (13-35, 15-30 hours),¹¹ reaching steady state in about 5 days. Once or twice daily dosing frequency may then be possible to improve dosing convenience and to minimize adverse effects from accumulation.
- ☰ Combining antiemetics aims to block several, but not overlapping, emetic pathways:
 - ☰ Initially, use of a single antiemetic drug up to maximum tolerated dose is preferable.
 - ☰ Single broader spectrum drugs such as methotrimeprazine and olanzapine have affinity at many receptors and may be as effective as, and easier for patients to handle than, multiple simultaneous antiemetics; may also minimize drug interactions.^{11, 19}
 - ☰ When combining antiemetics, polypharmacy risks are greater, as are adverse effects such as sedation and anti-cholinergic effects; monitor for overlapping toxicities.^{20, 21}
 - ☰ Avoid combinations with antagonistic actions as effectiveness of either is at risk:
 - ☰ Prokinetic agents such as metoclopramide are potentially antagonized by anticholinergics (e.g., dimenhydrinate, scopolamine, hyoscine).^{2, 8, 9, 11, 12}
 - ☰ Use combinations with different receptor affinities, e.g., dimenhydrinate and haloperidol,¹¹ or haloperidol with a 5HT₃ receptor antagonist such as ondansetron.¹⁹
- ☰ Corticosteroids may improve nausea caused by increased ICP (related to intracranial tumors), hypercalcemia of malignancy, malignant pyloric stenosis² or visceral causes ([see Underlying causes of nausea and vomiting in palliative care](#)); may also reverse partial bowel obstructions.
- ☰ Marijuana lacks controlled clinical efficacy studies; nabilone is an antiemetic alternative.¹
- ☰ Opioid-induced nausea lacks evidence of a preferred antiemetic choice.²² However, use of an antiemetic may help, thus increasing compliance with analgesic especially for patients sensitive to many drugs.
- ☰ Nausea might be minimized by switching opioids or route of administration.²²

Patient and family education

-  Explain that a combination of strategies may be needed, often due to multiple triggers.^{1,8}
-  Teach how to use non-oral medications and non-pharmacological methods.²
-  Encourage patients to continue analgesic medication as pain can make nausea worse.¹⁵
-  Offer tools to keep track of symptoms, medications taken and effectiveness.

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Resources specific to nausea and vomiting

- BC Cancer Agency Symptom Management Guidelines: Nausea
→ <http://www.bccancer.bc.ca/nursing-site/Documents/11.%20Nausea%20and%20Vomiting.pdf>
- BC Guidelines: Nausea and vomiting
→ http://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/palliative2_nausea.pdf
- BC's Heart Failure Network: Nausea and vomiting
→ <http://www.bcheartfailure.ca/wp-content/uploads/downloads/2015/01/Nausea-Vomiting-Jan-2015.pdf>

General Resources

- **Provincial Palliative Care Line** – for **physician** advice or support, call **1 877 711-5757** In ongoing partnership with the Doctors of BC, the toll-free Provincial Palliative Care Consultation Phone Line is staffed by Vancouver Home Hospice Palliative Care physicians 24 hours per day, 7 days per week to assist physicians in B.C. with advice about symptom management, psychosocial issues, or difficult end-of-life decision making.
- BC Centre for Palliative Care: Serious Illness Conversation Guide
→ <http://www.bc-cpc.ca/cpc/>
- BC Guidelines: Palliative Care for the Patient with Incurable Cancer or Advanced Disease
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care>
- BC Palliative Care Benefits: Information for prescribers
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program>
- National Centre for Complementary and Alternative Medicine (NCCAM) for additional information on the use of non-pharmacological interventions
→ <https://nccih.nih.gov/>
- Canadian Association of Psychosocial Oncology: Pan-Canadian Practice Guideline: Screening, Assessment and Management of Psychosocial Distress, Depression and Anxiety in Adults with Cancer
→ http://www.capo.ca/wp-content/uploads/2015/11/FINAL_Distress_Guideline1.pdf
- Fraser Health psychosocial care guideline
→ <https://www.fraserhealth.ca/media/psychosocial%20care.pdf>

Resources specific to health organization/region

- Fraser Health
→ <http://www.fraserhealth.ca/health-professionals/professional-resources/hospice-palliative-care/>

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- First Nations Health Authority
→ <http://www.fnha.ca/>
- Interior Health
→ <https://www.interiorhealth.ca/YourCare/PalliativeCare/Pages/default.aspx>
- Island Health
→ http://www.viha.ca/pal_eol/
- Northern Health
→ <https://www.northernhealth.ca/Professionals/PalliativeCareEndofLifeCare.aspx>
- Providence Health
→ <http://hpc.providencehealthcare.org/>
- Vancouver Coastal Health
→ <http://www.vch.ca/your-care/home-community-care/care-options/hospice-palliative-care>

Resources specific to patient population

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians
→ <https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf>
- ALS Society of British Columbia 1-800-708-3228
→ www.alsbc.ca
- BC Cancer Agency: Symptom management guidelines
→ <http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management>
- BC Renal Agency: Conservative care pathway and symptom management
→ <http://www.bcrenalagency.ca/health-professionals/clinical-resources/palliative-care>
- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management
→ <http://www.bcheartfailure.ca/for-bc-healthcare-providers/end-of-life-tools/>
- Canuck Place Children's Hospice
→ <https://www.canuckplace.org/resources/for-health-professionals/>
 - 24 hr line – 1.877.882.2288
 - Page a Pediatric Palliative care physician – 1-604-875-2161 (request palliative physician on call)
- Together for short lives: Basic symptom control in pediatric palliative care
→ http://www.togetherforshortlives.org.uk/professionals/resources/2434_basic_symptom_control_in_paediatric_palliative_care_free_download

UNDERLYING CAUSES OF NAUSEA AND VOMITING IN PALLIATIVE CARE

All underlying causes for this symptom have been outlined in the document.

See [next page](#) for medication related to causes

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| Chemical Cause | Key Features ^{2, 6, 7, 13, 20} | Antiemetic of Choice | Adverse Effects‡ |
|---|---|--|--|
| Drugs e.g., steroids, opioids Chemotherapy Metabolic e.g., hypercalcemia Toxins e.g., infection | Symptoms of drug toxicity or underlying disease. Nausea as predominant symptom. Nausea not relieved by vomiting. Delirium (suggests primary metabolic cause or metabolic derangement secondary to vomiting). Polydipsia and polyuria (suggests hypercalcemia or hyperglycemia). | 1st line: Haloperidol 0.5 to 1.5 mg PO/SC Q8H or 1.5 to 5 mg CSCI per 24 hours 2nd line: Methotrimeprazine 3.125 to 6.25 mg PO/SC Q8H or 6.25 to 25 mg CSCI per 24 hours 3rd line: Ondansetron 4 to 8 mg once or twice daily or 16 to 24 mg CSCI per 24 hours | QTc prolongation risk. Extrapyramidal symptoms (uncommon). QTc prolongation risk. Sedating at 12.5 mg per day and above. ²⁶ QTc prolongation risk. Constipation 11% ²⁷ (refer to Constipation guideline) Avoid IV ondansetron when using IV metoclopramide. ^{23,24} |
| Cortical Cause | Key Features | Antiemetic of Choice | Adverse Effects‡ |
| Anxiety Pain Previous nausea experience Emotional factors | Psychological or physical distress. Anticipatory nausea and vomiting. ¹³ | 1st line: Lorazepam 0.5 to 1mg sublingual QID PRN 2nd line: Methotrimeprazine 3.125 to 6.25 mg PO/SC Q8H or 6.25 to 25 mg CSCI per 24 hours 3rd line: Cannabinoids Nabilone 0.25 to 2 mg PO BID Medicinal cannabis ²⁵ | Sedation. QTc prolongation risk. Sedating at 12.5 mg per day and above. ²⁶ |

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| Cranial Cause | Key Features | Antiemetic of Choice | Adverse Effects‡ |
|---|---|--|--|
| Raised intracranial pressure (ICP) Meningeal infiltration Whole brain radiotherapy | Headache +/- cranial nerve signs, especially in the morning. Vomiting without nausea. Changes to vision and/or personality. Depressed consciousness (raised ICP). N&V in response to sensory stimulation (sights/sounds/smells) | <u>1st line:</u> Dimenhydrinate 50 mg PO/SC/PR Q4H to Q8H or 150 mg CSCI per 24 hours <u>1st line: Add</u> Dexamethasone 8 mg daily up to 8 mg bid PO/SC if raised ICP <u>2nd line: Haloperidol</u> 0.5 to 1.5 mg PO/SC Q8H or 1.5 to 5 mg CSCI per 24 hours <u>3rd line:</u> Methotrimeprazine 3.125 to 6.25 mg PO/SC Q8H or 6.25 to 25 mg CSCI per 24 hours | Sedation. QTc prolongation risk. Extrapyramidal symptoms (uncommon). QTc prolongation risk. Sedating at 12.5 mg per day and above. |
| Vestibular Cause | Key Features | Antiemetic of Choice | Adverse Effects‡ |
| Drugs e.g., opioids Motion sickness Tumor e.g., cerebellar, acoustic neuroma, cranial metastasis | Symptoms are movement related. Less common cause of nausea and vomiting. | <u>1st line: Dimenhydrinate</u> 50 mg PO/SC/PR Q8H or 150mg CSCI per 24 hours <u>2nd line: Scopolamine Transdermal</u> 1 to 2 patches applied to skin every 72 hours <u>3rd line:</u> Methotrimeprazine 3.125 to 6.25 mg PO/SC Q8H 6.25 to 25 mg CSCI per 24 hours Prochlorperazine 5-10 mg PO Q8H | Sedation. Anticholinergic effects, e.g., dry mouth. QTc prolongation risk. Sedating at 12.5 mg per day and above. ²⁶ |

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| Visceral or Serosal Cause | Key Features | Antiemetic of Choice | Adverse Effects† |
|--|--|---|--|
| Bowel obstruction Severe constipation Liver capsule stretch Ureteric distention Mesenteric metastases Pharyngeal stimulation (difficult expectoration) | Vomiting undigested food hours after ingestion (gastric outlet obstruction). Abdominal pain and altered bowel habit (intestinal obstruction). Pain may occur with oral intake. Vomitus may be large volume progressing from stomach contents, to bile to fecal matter (intestinal obstruction). | 1st line: <u>Dimenhydrinate</u> 50 mg PO/SC Q8H or 150 mg CSCI per 24 hours 2nd line: <u>Methotrimeprazine</u> 3.125 to 6.25 mg PO/SC Q8H 6.25 to 25 mg CSCI per 24 hours | Sedation. QTc prolongation risk. Sedating at 12.5 mg per day and above. ²⁶ |
| Gastric Stasis Cause | Key Features | Antiemetic of Choice | Adverse Effects† |
| Drugs e.g., opioids, tricyclics Tumor ascites Hepatomegaly Autonomic dysfunction Tumor infiltration | Impaired gastric emptying. Epigastric pain, fullness, acid reflux, early satiety, flatulence, hiccup. Intermittent nausea relieved by vomiting. | 1st line: <u>Metoclopramide*</u> 10 mg PO TID or QID before meals or 30 to 40 mg CSCI per 24 hours Higher doses should usually not be exceeded. ²⁴ 2nd line: Domperidone* 10 mg PO TID Health Canada recommends a maximum of 30 mg daily. ²³ | QTc prolongation risk. Extrapyramidal symptoms. ²⁸ QTc prolongation risk. ²⁸ |

† Off-label. PO = by mouth IV = Intravenous, SC = Subcutaneous, TID = three times daily, QID = four times daily ODT = oral dissolving tablet CSCI = continuous subcutaneous infusion.

*Adjust/monitor dosing in patients with renal dysfunction, avoid in complete bowel obstruction

‡QTc prolongation risk known to occur for domperidone, haloperidol, ondansetron, methotrimeprazine and is a conditional risk for metoclopramide use. Per <https://crediblemeds.org/>

Drug coverage and cost information available from: http://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/palliative2_nausea.pdf#page=5

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Consult most current product monograph for full drug information and adverse effects:
<https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>

Prices for prescription drugs may be obtained from BC PharmaCare. The British Columbia Palliative Care Benefits Plan <http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/palliative-formulary.pdf> provides province wide drug coverage for many of the recommended medications– check website to confirm coverage. **Consider price when choosing similarly beneficial medications, especially when the patient / family is covering the cost.**

NAUSEA AND VOMITING MANAGEMENT ALGORITHM - TITRATION⁹

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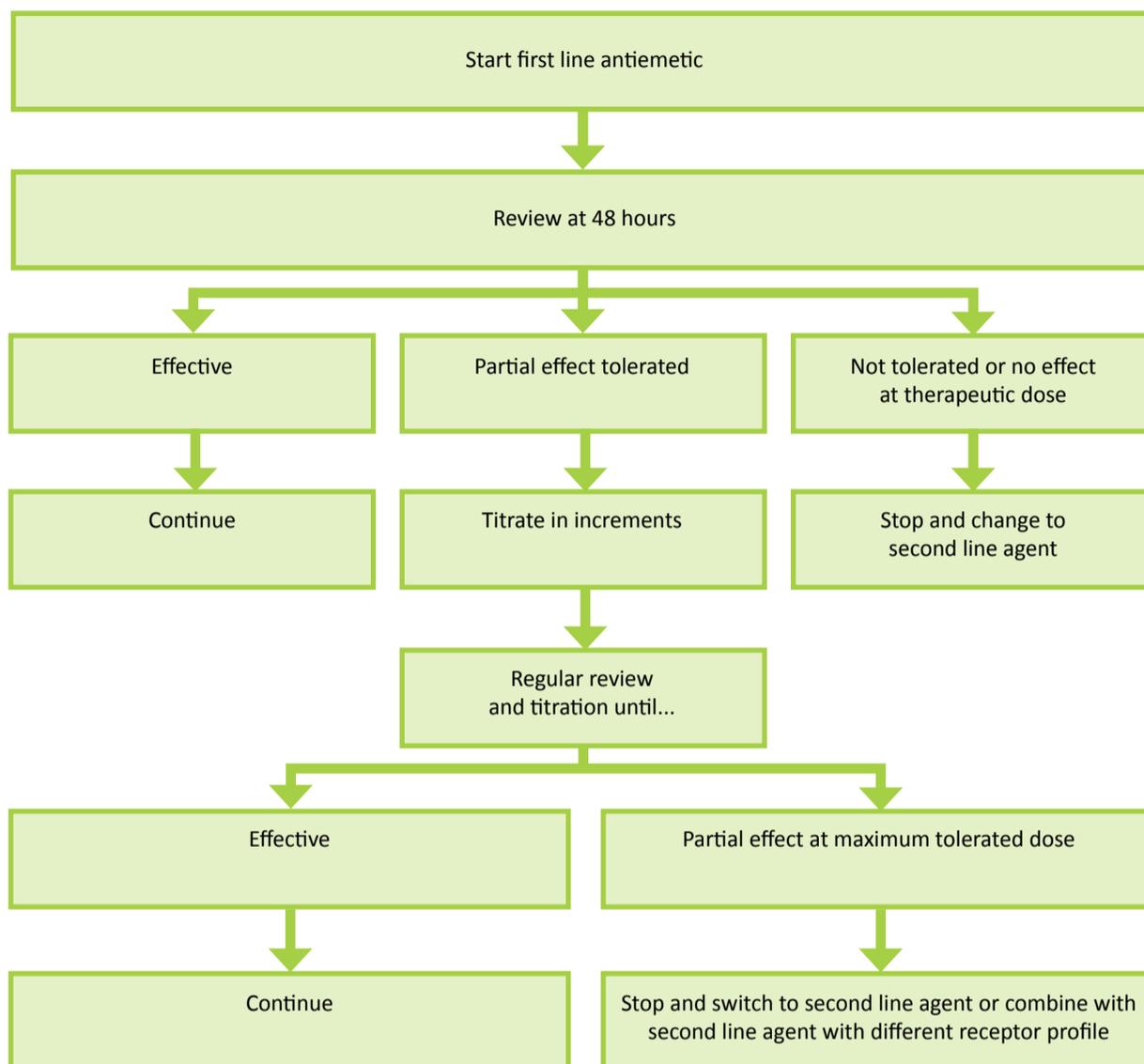
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NAUSEA AND VOMITING EXTRA RESOURCES OR ASSESSMENT TOOLS

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Antiemetics Oral Bioavailability's, Parenteral Dosing Adjustment^{14, 21, 23,30}

| Drug | Oral (PO) Bioavailability | Possible/Suggested Dosing Adjustment when switching from Oral to Subcutaneous or IV route of Administration‡ |
|-------------------|---------------------------|--|
| Dimenhydrinate | Not available* | Unknown, possibly by 50-100% |
| Haloperidol | 60 - 70 % | Reduce by 50-100 % |
| Lorazepam | 93 % | None |
| Metoclopramide | 50 - 80 % | Possibly reduce by 50-100 % |
| Methotrimeprazine | 20 - 40% | Reduce by 50% |
| Ondansetron | 56 - 71 % | None |
| Olanzapine | 60 % | Possibly reduce by 50-100 % |

*Dimenhydrinate is a 53 to 56% component of diphenhydramine³⁰ and the latter has a 42% oral bioavailability.¹⁴

‡The need to adjust dosing is poorly studied for these antiemetics, while use of small doses may partially preclude dosing adjustments for oral to parenteral dosing.³¹ Studies to guide rationale dosage reduction when changing between oral and parenteral routes with antiemetics are lacking, however known oral bioavailability data and some expert opinion suggest that dose adjustments may need to be considered and therapy individualized.

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DEFINITION

Dysphagia is defined as difficult swallowing and is typically classified as **oropharyngeal** or **esophageal**¹⁻³; both may result in coughing, choking, or a sensation of choking, regurgitation and aspiration.

Oropharyngeal or transfer dysphagia is characterized by difficulty initiating a swallow. This may be accompanied by a sensation of residual food remaining in the pharynx.²

Esophageal dysphagia is difficulty swallowing several seconds after initiating a swallow followed by a sensation of food getting stuck in the esophagus when the food bolus fails to easily transverse the esophagus.^{2,3}

PREVALENCE

Swallowing disorders are part of the natural process at the end of life, irrespective of the etiology.⁴ Dysphagia in the geriatric population is estimated at 10-15%.¹ Oropharyngeal dysphagia in patients with dementia may be as high as 93%.⁵ High-risk groups include: persons who have suffered a cardiovascular accident (25-40%); persons with Parkinson's disease (50-80%),³ and advanced multiple sclerosis (34%).⁵ More than 70% of esophageal cancer patients have experienced dysphagia at time of diagnosis.³

IMPACT

Dysphagia carries a high risk of aspiration and respiratory complications, malnourishment and dehydration and, as a result, poorer survival than people without dysphagia.^{3,6} Chronic dysphagia can be both frustrating and frightening for patients. Aspiration may cause pneumonia, fevers, malaise, shortness of breath and, in rare cases, death^{2,5}; choking causes distress for both patient and care providers alike. Dysphagia may lead to social isolation and fear of choking to death in public. Dysphagia is a pivotal symptom that can prompt goals of care to become more focused on palliation.⁵

STANDARD OF CARE

Step 1 | Goals of care conversation

Determine goals of care in conversation with the patient, family and interdisciplinary team. Refer to additional resources ([Additional resources for management of dysphagia](#)) for tools to guide conversations and required documentation. Goals of care may change over time and need to be reconsidered at times of transition, e.g., disease progression or transfer to another care setting.

Step 2 | Assessment

Dysphagia Assessment: Using Mnemonic O, P, Q, R, S, T, U and V³⁵

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| Mnemonic Letter | Assessment Questions <i>Whenever possible, ask the patient directly. Involve family as appropriate and desired by the patient.</i> |
|-------------------------------|---|
| O nset | When did it begin? How long does it last? How often does it occur? |
| P rovoking /Palliating | What foods or fluids are more difficult to swallow? Which ones are easier? What brings it on? What makes it better? What makes it worse? Does changing position help? |
| Q uality | What does it feel like? Can you describe it? |
| R egion/Radiation | Not applicable |
| S everity | How severe is this symptom? What would you rate it on a scale of 0-10 (0 being none and 10 being the worst possible)? Right now? At worst? On average? How bothered are you by this symptom? Are there any other symptom(s) that accompany this symptom (e.g. nausea, cough, dyspnea)? |
| T reatment | What medications and treatments are you currently using? Are you using any non-prescription treatments, herbal remedies, or traditional healing practices? How effective are these? Do you have any side effects from the medications and treatments? What have you tried in the past? Do you have concerns about side effects or cost of treatments? |
| U nderstanding | What do you believe is causing this symptom? How is it affecting you and/or your family? What is most concerning to you? How is this affecting your intake of food and fluid? |
| V alues | What overall goals do we need to keep in mind as we manage this symptom? What is your acceptable level for this symptom (0-10)? Are there any beliefs, views or feelings about this symptom that are important to you and your family? What is the cultural or spiritual significance of food in your family? |

Symptom Assessment: Physical assessment as appropriate for symptom

- Investigations include taking a history and examining the oral cavity, head, neck, and supraclavicular region.
- Check for oropharyngeal thrush which can predispose to candida esophagitis.
- Neurologic examination includes testing of all cranial nerves involved in swallowing (V, VII, IX, XI, and XII).⁹

Diagnostics: consider goals of care before ordering diagnostic testing

- Investigations are conducted in alignment with prognosis, patient condition and goals of care conversations^{2, 7, 8}. Focused instrumental evaluation can involve videofluoroscopic or endoscopic evaluation of swallowing or barium swallow conducted by a qualified professional.

Step 3 | Determine possible causes and reverse as possible if in keeping with goals of care (For more details, see [Possible pharmacological causes or contributors to dysphagia in palliative care](#))

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Dysphagia etiologies are multifactorial. Many progressive diseases lead to unsafe and inefficient swallowing: see below. Further, there are 160 known medications with dysphagia specified as a potential adverse effect.⁵ (See [Possible pharmacological causes or contributors to dysphagia in palliative care](#) for a list of medication causes.)

Other causes of dysphagia³

Oropharyngeal

- **Structural:** malignancy, enlarged thyroid, Zenker's diverticulum
- **Neurological:** CVA, amyotrophic lateral sclerosis, brainstem tumours, bulbar poliomyelitis, multiple sclerosis, Parkinsonism, neuropathy (diabetes, alcohol, cachexia), dementias
- **Myopathic:** dermatomyositis, muscular dystrophy, polymyositis, myasthenia gravis, thyroid disease,
- **Iatrogenic:** medications that result in a myopathy or that inhibit saliva (See [Possible pharmacological causes or contributors to dysphagia in palliative care](#) for examples), radiotherapy to the head and neck, surgical procedures of the head and neck
- Poor dentition
- Anxiety

Esophageal

- **Neuromuscular:** achalasia, oesophageal spasm, scleroderma, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel diseases
- **Vascular:** ischaemic esophagus
- **Structural:** stricture secondary to reflux, diverticula, malignancy (esophageal, gastric), benign tumours, external vascular compression, mediastinal masses, foreign body, mucosal injury secondary to infections, allergic disorders (eosinophilic oesophagitis), mucosal injury secondary to skin disorders (pemphigus vulgaris, pemphigoid, epidermolysis bullosa dystrophica)

PRINCIPLES OF MANAGEMENT



When considering a management approach, always balance burden of a possible intervention against the likely benefit (e.g., does the intervention require transfer to another care setting?)

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- Management strategies differ depending upon whether the problem is localized to the oropharynx or the esophagus, the chronicity of the underlying disease, and the overall prognosis.³
- The goals of therapy are to mitigate risk and discomfort, and to maximize quality of life, for the patient.¹
- Anticipate swallowing difficulty with approaching end of life. Lessen the swallowing burden by stopping medications where possible, temporarily or permanently
- Review medication profile for those drugs that may cause or contribute to impaired swallowing; eliminate any that are unnecessary. See ([Possible pharmacological causes or contributors to dysphagia](#))
- Ensure alternate administration routes available to maintain symptom control
- Minimize dysphagia difficulties using medication administration strategies
- Optimize care by involvement of an interdisciplinary team:
 - A qualified dysphagia professional which may be an SLP, OT, RD to provide expert assessment and management of communication and swallowing disorders ¹⁰
 - A dietician to provide expert food and fluids selection and consistency modification. ^{4, 11}

Step 4 | Interventions

LEGEND FOR USE OF BULLETS

Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence, using a modified GRADE process.

| | |
|--|--|
|  | Use with confidence: recommendations are supported by moderate to high levels of empirical evidence. |
|  | Use if benefits outweigh potential harm: recommendations are supported by clinical practice experience, anecdotal, observational or case study evidence providing low level empirical evidence. |
|  | Use with caution: Evidence for recommendations is conflicting or insufficient, requiring further study |
|  | Not recommended: high level empirical evidence of no benefit or potential harm |

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Interventions which may be available in the home and residential care facilities

-  **Consultation** with a qualified dysphagia professional, if available
-  Positioning
-  **Safe swallowing** methods
-  Consistent **oral care**
-  **Environmental** adaptations
-  Oral **feeding** modifications
-  **Medication** administration adaptations
-  Compensatory **postural changes**

Interventions requiring additional equipment or admission to acute care

-  **Malignant esophageal strictures** can be palliated with a combination of dilatation, stent placement, and adjuvant radiotherapy or brachytherapy. Patient prognosis and goals of care determines selection.³ Consult with an oncologist.

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No pharmacological agents have evidence to directly benefit oropharyngeal swallowing function.^{4, 5, 13}

Medications can contribute to or cause dysphagia by affecting all stages of swallowing¹⁴ and are one of the most readily corrected causes of dysphagia.¹⁵

-  Drugs may induce adverse effects that include: dry mouth, impaired muscle function, loss of sensory control, taste and smell impairment, sedation/confusion, immunosuppression (predisposing to fungal, viral bacterial infections), and gastric reflux from a lowered esophageal sphincter tone or sialorrhea.
-  Avoid polypharmacy.¹³
-  Avoid drugs that may contribute to impaired swallowing. ([Possible pharmacological causes or contributors to dysphagia in palliative care](#))
-  Modify medication route to use alternate routes. Can be required in up to 50% of patients,¹⁶ e.g., options include changing to:
 -  Commercially available liquids, orodispersible tablets, or specialty compounded suspensions.
 -  Transdermal, parenteral, sublingual, buccal, rectal and intranasal routes.
-  Consult pharmacist for assistance with changes, product suitability, availability, costs.¹¹
-  Improve oral medication administration strategies.
-  Support use of drugs for symptoms frequently occurring in dysphagia patients:
 -  Gastric reflux may benefit from the use of proton pump inhibitors, antacids, prokinetics for dysmotility, or barrier therapy with sucralfate.^{3, 5}
 -  Use opioids or NSAIDs for temporary pain from esophageal stent insertion.^{17, 18}

Patient and family education

-  Describe benefits and risks of various feeding options in order to make informed decisions.⁵
-  Explain risks and consequences of aspiration pneumonia while recognizing some will choose to eat at risk.
-  Describe any specific diet, rationale, manner of food modification and positioning techniques that best serve the patient.⁵
-  Promote slow, small bolus sizes to prevent choking.
-  Emphasize the importance of allowing patients to enjoy their intake with minimal restrictions in last days of life.¹²
-  Continue to include the patient in the social and spiritual aspect of gatherings around food, especially culturally significant feasts or spiritual practices.

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Resources specific to dysphagia

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians: Dysphagia
→ <https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf>
- BC Cancer Agency Symptom management guidelines: Dysphagia
→ <http://www.bccancer.bc.ca/nutrition-site/Documents/Symptom%20management%20guidelines/Dysphagia.pdf>

General Resources

- **Provincial Palliative Care Line** – for **physician** advice or support, call **1 877 711-5757** In ongoing partnership with the Doctors of BC, the toll-free Provincial Palliative Care Consultation Phone Line is staffed by Vancouver Home Hospice Palliative Care physicians 24 hours per day, 7 days per week to assist physicians in B.C. with advice about symptom management, psychosocial issues, or difficult end-of-life decision making.
- BC Centre for Palliative Care: Serious Illness Conversation Guide
→ <http://www.bc-cpc.ca/cpc/>
- BC Guidelines: Palliative Care for the Patient with Incurable Cancer or Advanced Disease
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care>
- BC Palliative Care Benefits: Information for prescribers
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program>
- National Centre for Complementary and Alternative Medicine (NCCAM) for additional information on the use of non-pharmacological interventions
→ <https://nccih.nih.gov/>
- Canadian Association of Psychosocial Oncology: Pan-Canadian Practice Guideline: Screening, Assessment and Management of Psychosocial Distress, Depression and Anxiety in Adults with Cancer
→ http://www.capo.ca/wp-content/uploads/2015/11/FINAL_Distress_Guideline1.pdf
- Fraser Health psychosocial care guideline
→ <https://www.fraserhealth.ca/media/psychosocial%20care.pdf>

Resources specific to health organization/region

- Fraser Health
→ <http://www.fraserhealth.ca/health-professionals/professional-resources/hospice-palliative-care/>

Additional resources for management of dysphagia continued on [next page](#)

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- First Nations Health Authority
→ <http://www.fnha.ca/>
- Interior Health
→ <https://www.interiorhealth.ca/YourCare/PalliativeCare/Pages/default.aspx>
- Island Health
→ http://www.viha.ca/pal_eol/
- Northern Health
→ <https://www.northernhealth.ca/Professionals/PalliativeCareEndofLifeCare.aspx>
- Providence Health
→ <http://hpc.providencehealthcare.org/>
- Vancouver Coastal Health
→ <http://www.vch.ca/your-care/home-community-care/care-options/hospice-palliative-care>

Resources specific to patient population

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians
→ <https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf>
- ALS Society of British Columbia 1-800-708-3228
→ www.alsbc.ca
- BC Cancer Agency: Symptom management guidelines
→ <http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management>
- BC Renal Agency: Conservative care pathway and symptom management
→ <http://www.bcrenalagency.ca/health-professionals/clinical-resources/palliative-care>
- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management
→ <http://www.bcheartfailure.ca/for-bc-healthcare-providers/end-of-life-tools/>
- Canuck Place Children's Hospice
→ <https://www.canuckplace.org/resources/for-health-professionals/>
 - 24 hr line – 1.877.882.2288
 - Page a Pediatric Palliative care physician – 1-604-875-2161 (request palliative physician on call)
- Together for short lives: Basic symptom control in pediatric palliative care
→ http://www.togetherforshortlives.org.uk/professionals/resources/2434_basic_symptom_control_in_paediatric_palliative_care_free_download

POSSIBLE PHARMACOLOGICAL CAUSES OR CONTRIBUTORS TO DYSPHAGIA IN PALLIATIVE CARE^{1, 5, 14, 19-27}

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As there is only *an association* of risk of contributing to swallowing impairment, and no evidence from randomized placebo-controlled studies, often consider stopping drugs temporarily or permanently. Consult other healthcare professionals, such as pharmacists, for review and information assistance.

| Medication-Induced Esophageal Mucosa Injury | Drug Induced Adverse Effects | |
|---|---|---------------------------------|
| • Alendronate | Dry Mouth | Loss of Sensory Control |
| • Alcohol | • Anticholinergics (e.g., atropine) | • Local anesthetics |
| • Aripiprazole | • Antidepressants | Peristalsis, Motility Reduction |
| • ASA | • Antiemetics | • Anticholinergics |
| • Carbamazepine | • Antihistamines | • Antihistamines |
| • Clindamycin | • Bronchodilators | • Antipsychotics |
| • Chemotherapy (e.g., vincristine) | • Diuretics | Sedation or Confusion |
| • Corticosteroids (e.g., prednisone) | • Supplemental oxygen | • Antiepileptics |
| • Dantrolene | Esophageal Sphincter Tone Lowered (increases reflux) | • Anxiolytics (e.g., lorazepam) |
| • Digoxin | | • Benzodiazepines |
| • Doxycycline | • Anticholinergics | • Opioids |
| • Everolimus | • Benzodiazepines | • Skeletal muscle relaxants |
| • Iron containing products | • Calcium channel blockers | Sialorrhea (Saliva Excess) |
| • Macrolide antibiotics | • Isosorbide dinitrate | • Ketamine ²³ |
| • Morphine | • Opioids | • Olanzapine (6%) |
| • NSAIDs e.g., ibuprofen | • Theophylline | • Risperidone (1-10%) |
| • Olanzapine | Immunosuppression | • Ziprasidone (4%) |
| • Oxybutynin | • Azathioprine | Taste or Smell Impairment |
| • Phenobarbital | • Chemotherapy (e.g., paclitaxel) | • Oxybutynin (1-5%) |
| • Potassium chloride | • Corticosteroids, oral inhaled (increased risk of candidiasis) | • Phenytoin |
| • Selegiline | | • Sunitinib (21%) |
| • Tetracycline (pH of 1.6-3.2) | • Cyclosporine | • Testosterone (5.8% smell) |
| • Trimethoprim-Sulfamethoxazole | Impaired Muscle Function | • Topiramate (2-8%) |
| • Vitamin C (ascorbic acid) | • Anticholinergics | • Zopiclone |
| | • Antipsychotics | • Phenobarbital |
| | • Corticosteroids (muscle wasting) | |
| | • Skeletal muscle relaxants | |
| | • Neuromuscular blocking agents | |
| | • Statins | |

This table provides examples; up to 160 medications may contribute to swallowing disorders.^{14, 20}

MEDICATIONS FOR MANAGEMENT OF DYSPHAGIA

Information on medications is included within this document.

Prices for prescription drugs may be obtained from BC PharmaCare. The British Columbia Palliative Care Benefits Plan <http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/palliative-formulary.pdf> provides province wide drug coverage for many of the recommended medications—check website to confirm coverage. **Consider price when choosing similarly beneficial medications, especially when the patient / family is covering the cost.**

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DYSPHAGIA MANAGEMENT ALGORITHM

No management algorithm included in this document.

DYSPHAGIA EXTRA RESOURCES OR ASSESSMENT TOOLS

Oral Medication Administration Strategies for Dysphagia Patients

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| Strategy | Comment |
|--|---|
| Formulation Assessment | |
| Switch from an oral capsule formulation to a tablet. | Gelatin capsules are more likely to stick to esophageal mucosa causing ulcerogenic harm (e.g., doxycycline). ²⁷ |
| Pick a suitable tablet size. | 7 to 9 mm reported as the easiest size of tablet to swallow. ²⁸ |
| Switch to multiple, smaller doses of tablets or capsules. | Change from a larger bulky strength to an equal multiple of smaller doses. |
| Switch to a lighter oral formulation (e.g., immediate release). | Sustained release formulations tend to be bulky and prone to harmful lodging in the esophagus. ²⁷ |
| Consider shape of tablet or capsule. | Oval (versus round) may help. Not certain; one study found no difference comparing versus oblong and capsule. ^{15, 29} |
| Faster dissolving/disintegrating. | New formulations dissolve or disintegrate in mouth. ²⁷ |
| Timing of Administration | |
| Take in the morning. | When you are more likely upright than near bedtime. ¹⁵ |
| Take when functioning best. | Best swallowing functioning could be later in the day. ⁴ |
| Reduce dosing frequency. | Assess if can be given less frequently (e.g., once daily). ²⁷ |
| At least 30 minutes before HS. | Suggested safer taking 30 minutes prior to sleeping. ¹⁵ |
| Avoid oral tablet and capsule doses when sleeping. | Less saliva production, esophageal motility when sleeping. Greater risk of immediately lying back down. ^{15, 27} |
| Positioning | |
| Sit up when taking the medication. | Sit upright, 45 to 90 degrees for intake, and head upright. ¹⁵ |
| Take at least 10 minutes before lying down (reclining). | Avoid recumbent position for at least 10 minutes, safer still 30 minutes . Improves esophageal medication clearance. ^{15, 27} |
| Reposition head when swallowing. | For example, chin tuck posture, head tilt. Ask SLP for assistance. ^{4, 5, 9} |
| Pre-dose Preparation | |
| | Use a preliminary lubricating swallow/sip of water pre-dose. ²⁷ |
| At time of administration | |
| Take with <u>sufficient</u> water. | Give 100 mL (to 250 mL) post-dose. Wet swallows have greater amplitude and duration of contraction than dry. ^{19, 27} |
| Other Strategies | |
| Avoid medication errors. | Medication error rate is much higher (21.1%) in dysphagia patients than others (5.9%). Administer using great care. ³⁰ |
| Switch to a liquid formulation. | To stomach quicker, spares esophagus mucosa from prolonged tablet contact. Ensure consistency not "too thin". ²⁷ |
| Change to a drug with a lower side effect risk, or lower dose. | For example, consider a trial switch to a neuroleptic with a lower anticholinergic effect. Or try lower dose. ^{27, 31} |
| Shorten length of therapy. | To minimize causation risk. ²⁷ |
| Avoid rushing to crush. | Assess if drug is classified "hazardous" or suitable to crush. ^{11, 32} |
| Thickeners. | Medication compatibility, absorption effects unknown. ^{11, 33} |
| Mixing into food (e.g., apple sauce or ice-cream). | Drug-food compatibilities are unknown so when combining with crushed medications, mix and administer immediately. ⁴ |
| Proactive medication availability planning in event of inability to swallow. | Plan for future non-oral medication options; may need suddenly. At home, palliative drugs kits are helpful, where available. ³⁴ |

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DEFINITION

Anorexia is the loss or absence of appetite^{1,2} leading to reduced caloric intake,^{3,4} resulting in loss of weight and fat tissue.^{5,6} **Cachexia** is the involuntary loss of more than 10% of pre-morbid weight,^{1,7} resulting in loss of muscle, with or without loss of fat.^{4,6,8-11} It is a chronic hypercatabolic, inflammatory state and cannot be entirely attributed to poor caloric intake.^{2,12} Cachexia is not reversible and may not correlate with anorexia.^{1,8,13} Anorexia and cachexia are different clinical syndromes and do not always co-exist; however, they often occur together in advanced cancer and serious chronic illness.⁶ **Anorexia-cachexia syndrome (ACS)** is a complex, multi-factorial metabolic syndrome¹¹ characterised by anorexia, cachexia,¹⁴ asthenia, fatigue,¹⁵ functional decline and change in body image.⁷

PREVALENCE

Anorexia is common among patients with advanced cancer and other life-limiting chronic diseases.¹⁶⁻¹⁸ It occurs in 26% of palliative patients,¹⁹ 66% of cancer patients,²⁰ and is more common in the elderly. Cachexia occurs in more than 80% of patients with cancer before death¹⁵ and in 12-85% of patients with other conditions.²¹⁻²⁴ It is the main cause of death in more than 20% of patients.^{7,25,26} Anorexia-cachexia syndrome occurs in up to 86% of cancer patients²⁷ (particularly lung, pancreas and gastric) and in a variety of chronic diseases, including 10-60% in acquired immunodeficiency syndrome (AIDS), 16-36% in congestive heart failure (CHF), 30-70% in chronic obstructive pulmonary disease (COPD),^{28,29} and 30-60% in chronic kidney disease (CKD),³⁰ rheumatoid arthritis (RA), and dementia.^{4,7,17,25,31-38}

IMPACT

Anorexia can lead to poor caloric intake and protein-calorie malnutrition; it is reversible when causes are corrected.^{6,39,40} People assume that anorexia causes cachexia but, in many cases, it is the reverse.⁴¹ Anorexia-cachexia syndrome (ACS) leads to serious physical and functional deficits, increased dependency, and impaired quality of life (QOL).^{14,42} ACS increases risk of hospitalization,^{43,44} may prevent further interventions such as surgery or chemotherapy,¹ and is an indicator of poor prognosis.^{7,18,45}

The stigma of “wasting” and the symbolism of “feeding as caring” create significant emotional and social distress for both ACS patients and family.⁴⁶⁻⁴⁸ Patients suffer devastating loss of body image and self-esteem,¹⁵ anxiety and depression,⁴⁶ and can withdraw socially. Caregivers become anxious and distressed, feeling helpless and guilty as they perceive their loved one as “starving to death”.^{1,49} Well-meaning pressure to eat creates tension and conflict with the person who is unable.^{15,50-54} Forcing food when the body can’t handle it creates discomfort and can make other symptoms more difficult to manage.⁴¹

STANDARD OF CARE

Step 1 | Goals of care conversation

Determine goals of care in conversation with the patient, family and interdisciplinary team. Refer to additional resources ([Additional resources for management of anorexia](#)) for tools to guide conversations and required documentation. Goals of care may change over time and need to be reconsidered at times of transition, e.g., disease progression or transfer to another care setting.

Step 2 | Assessment

Anorexia Assessment: Using Mnemonic O, P, Q, R, S, T, U and V¹

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| Mnemonic Letter | Assessment Questions <i>Whenever possible, ask the patient directly. Involve family as appropriate and desired by the patient.</i> |
|-------------------------------|---|
| O nset | When did your appetite loss begin? How long does it last? How often does it happen? Have you lost weight? |
| P rovoking /Palliating | Have you noticed anything that brings on a loss of appetite? What makes your appetite better? What makes it worse? How have you adjusted the types of food you eat? |
| Q uality | How much weight have you lost? Do you have any fatigue, weakness or loss of abilities? Can you describe how you feel when you think about eating? |
| R egion/Radiation | Not applicable |
| S everity | How severe is your appetite loss? What would you rate it on a scale of 0-10 (0 being none and 10 being the worst possible)? Right now? At worst? On average? How bothered are you by your appetite loss? How much weight have you lost over what period of time? Are there other symptoms that accompany your lack of appetite (e.g., nausea, dysphagia, or fatigue)? |
| T reatment | What medications and treatments are you currently using to improve your appetite? Are you using any non-prescription treatments, herbal remedies, or traditional healing practices? How effective are these? Do you have any side effects from the medications and treatments? What have you tried in the past? Do you have concerns about side effects or cost of treatments? |
| U nderstanding | What do you believe is causing your decreased appetite and/or weight loss? How does this impact your daily activities, ability to function, sleep, your sense of well-being? How is it affecting you and/or your family? What is most concerning to you? |
| V alues | What overall goals do we need to keep in mind as we manage this symptom? What are your expectations? Given that it may not be possible to improve your appetite or reverse weight loss, what is most important to your quality of life? What is your acceptable level for this symptom (0-10)? Are there any beliefs, views or feelings about this symptom that are important to you and your family? |

Symptom Assessment: Physical assessment as appropriate for symptom

Diagnostics: consider goals of care before ordering diagnostic testing

Identify risk factors that compromise nutrition access or intake.^{18, 71} Disease progression tends to continue with functional decline, increasing fatigue, anorexia, and cachexia.⁷⁰ Tests may reduce patient's quality of life.⁶ Not necessary to weight patients routinely in last stages of illness.

- Lab tests: CBC, electrolytes, glucose, TSH and serum albumin.^{4, 40, 72}

Step 3 | Determine possible causes and reverse as possible if in keeping with goals of care (For more details, see [Underlying causes of anorexia in palliative care](#))

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Anorexia has numerous causes, many of which are reversible; anorexia doesn't cause cachexia. Cachexia causes anorexia, which then worsens cachexia.⁴¹

- Primary causes relate to changes (metabolic and neuroendocrine) directly associated with underlying disease and inflammatory state.
- Secondary contributing factors (fatigue, pain, dyspnea, infection, etc.) lead to weight loss.^{33-35, 38, 55-57, 73-76} (See [Underlying causes of anorexia in palliative care](#))

PRINCIPLES OF MANAGEMENT



When considering a management approach, always balance burden of a possible intervention against the likely benefit (e.g., does the intervention require transfer to another care setting?)

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- Determine food intake, impact on patient performance, and potential for reversal.¹¹
- Identify, and where appropriate with goals of care, treat reversible causes of anorexia.^{14, 77} (See [Underlying causes of anorexia in palliative care](#)) Cachexia is not reversible.²
- Offer information and practical advice about nutrition, diet and managing anorexia.^{14, 77}
- In early stages, aim to restore or maintain nutritional and functional status.^{14, 78}
- In later stages, focus on patient comfort and reducing patient and family anxiety.⁷⁷
- Involve interdisciplinary team including dietician, physiotherapist, occupational therapist, pharmacist, speech and language pathologist, cultural and spiritual care.^{6, 77}
- Acknowledge distress about body image, fatigue and functional decline.^{14, 77}
- Establish realistic goals.⁴

Step 4 | Interventions

LEGEND FOR USE OF BULLETS

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Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence, using a modified GRADE process.

| | |
|--|--|
|  | Use with confidence: recommendations are supported by moderate to high levels of empirical evidence. |
|  | Use if benefits outweigh potential harm: recommendations are supported by clinical practice experience, anecdotal, observational or case study evidence providing low level empirical evidence. |
|  | Use with caution: Evidence for recommendations is conflicting or insufficient, requiring further study |
|  | Not recommended: high level empirical evidence of no benefit or potential harm |

Non-pharmacological interventions

Interventions available in the home and residential care facilities

-  **Consultation with dietician (811 HealthLink)** for education and recommended supplements⁶
-  **Oral nutrition support** may be helpful early in the disease process.⁶ Evidence of effect in COPD patients.⁷⁹ No benefit shown in cancer patients.^{15, 17, 25, 80, 81}. Consider the cost of nutritional supplements as a potential barrier.
-  **Physical exercise** may prevent or slow loss of lean body mass to help patients maintain independence longer.⁸² Evidence is insufficient to determine safety or effectiveness in the cancer population. Studies are in progress.⁸³
-  **EPA fish oils** containing omega3 fatty acid. Some studies suggest role to stabilize weight loss and promote weight gain. Poor palatability.⁴²

Interventions requiring additional equipment or admission to acute care

-  **Enteral (tube) feeding** may benefit a sub-set of patients when reduced intake is due to structural/functional causes if appetite is intact and if reasonable quality of life. Gastrostomy tubes are preferred to NG tubes; also helps drainage in complete bowel obstruction.^{6, 33, 34, 76, 84-89}
-  **Enteral (tube) feeding** is NOT recommended to manage weight loss in advanced progressive illnesses such as cancer, heart failure, lung failure, cystic fibrosis, multiple sclerosis, motor neuron disease, Parkinson's disease, dementia and AIDS.⁹⁰ Evidence does not show improved quality of life, healing, reduced pressure ulcers, enhanced functional capacity, or increased survival⁸⁸ in this patient population.
-  **Total parental nutrition** NOT recommended: small benefit, increased risk of infection, reduced survival.⁷

Pharmacological interventions

(Refer to [Medications for management of anorexia](#))

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Review causative drugs, objectives

-  Assess if drugs could be a cause of anorexia, taste or smell alteration.
-  Stop unnecessary drugs; appropriately consider trial dose reduction/ stoppage of suspected drug causes or a switch to drug option of lower anorexic propensity.
-  Before starting drugs for anorexia, align appetite stimulants with goals of care as they have minimal or no demonstrated influence on quality of life^{38, 40, 91-93} and often do not reverse cachexia.⁹⁴ Cachexia improvement, even if treated, has limited improvement impact on quality of life,⁹² no effect on lean body mass,^{38, 40} modest effect on weight gain,^{93, 95} does not improve survival.^{4, 38, 91, 95}

Pharmacological management appropriate for secondary contributing symptoms

-  Medications can be useful to treat secondary causes of anorexia^{5, 6, 40, 96, 97} including: metoclopramide or domperidone for early satiety, nausea/ vomiting, gastroparesis; mirtazapine or antidepressants for depression; antifungals for oral or esophageal candidiasis. Refer to [Medications for management of anorexia](#) for doses.
-  Anorexia may also be improved with drug treatment of other secondary symptomatic causes including pain. Refer to other guidelines for management.

Anorexia Treatment Management

-  **Megestrol acetate** - start with 160 mg PO daily; is as effective as higher doses for anorexia.^{40, 91, 98} Larger doses may benefit cachexia, up to 800 mg daily.
 -  Appetite stimulation demonstrated in advanced cancer and AIDs patients; some effectiveness for COPD, ESRD, and other pathologies.^{11, 40, 94}
 -  Usually well-tolerated, edema occasionally.^{11, 93} Thromboembolism, such as deep vein thrombosis, is infrequent but concerning as has resulted in death.^{93, 94, 96} This risk may be greater in elderly with impaired mobility.⁹⁹
-  **Corticosteroids** stimulate appetite in 60-80% of patients.^{97, 100} Studies show a similar effectiveness to megestrol.^{38, 91, 101} Effect can occur within a few days,⁹⁷ with a significant effect from 2 up to 8 weeks,^{102, 103} but may disappear after 3 to 4 weeks.^{102, 104}
-  **Stop dexamethasone** trial if up to 4 mg daily dose fails to improve appetite within 7 to 10 days.^{97, 104, 105} Use beyond 6 to 8 weeks is not recommended as adverse effects dramatically increase with duration of use.^{103, 106} Consider megestrol as an alternative.^{94, 107}

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Pharmacological interventions *continued*

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Other appetite stimulants

-  **Cannabinoids** have not shown consistent appetite improvement in studies.^{91, 94} Central nervous system side effects limit patient use acceptability.⁶
-  **Marijuana** stimulates appetite according to anecdotal reports.^{40, 91, 108} Review current use regulations as appropriate, such as for medicinal marijuana.¹⁰⁹
-  **Mirtazapine**, an antidepressant, may improve appetite and weight in cancer-associated anorexia and is well tolerated; results are limited and use awaits further study.^{40, 91, 110}
-  **Not recommended:** hydrazine sulfate,^{91, 94} Eicosapentaenoic acid (or fish oil supplementation),^{40, 42, 91, 111} thalidomide^{40, 91, 112, 113} combinations of drugs.^{11, 40, 91}

Patient and family education

Teach patients and families about the natural progression of disease^{4, 6, 14}:

-  Explain metabolic abnormalities are causing the anorexia.¹
-  Give early nutritional counselling.¹ Some patients may benefit from nutritional supplementation or appetite stimulation but this does not reverse the underlying process.
-  Gradual reduction in oral intake is a natural part of the illness; it is not starvation.^{14, 40}
-  Give patient permission to eat less and educate family to reduce focus on food.⁷⁷ Encourage alternate forms of caring (massage, oral care, reading, presence)
-  Focus on enjoyment of food within limits of patient ability; encourage social interaction.¹⁴ Include the patient in social gatherings even if they do not feel like eating.
-  Offer small frequent meals high in calories, attractively presented; favorite foods and rest before meals may be helpful.⁴⁰ Tasting can be enjoyable.
-  Previous dietary restrictions, except those for allergy, may be relaxed.¹⁴

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Resources specific to Anorexia

- BC Cancer Agency Symptom management guidelines: Anorexia and Cachexia
→ <http://www.bccancer.bc.ca/nursing-site/Documents/2.%20Anorexia%20and%20Cachexia.pdf>
- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management: Anorexia and cachexia
→ <http://www.bcheartfailure.ca/wp-content/uploads/downloads/2015/01/Anorexia-and-Cachexia-Jan-20151.pdf>

General Resources

- **Provincial Palliative Care Line** – for **physician** advice or support, call **1 877 711-5757** In ongoing partnership with the Doctors of BC, the toll-free Provincial Palliative Care Consultation Phone Line is staffed by Vancouver Home Hospice Palliative Care physicians 24 hours per day, 7 days per week to assist physicians in B.C. with advice about symptom management, psychosocial issues, or difficult end-of-life decision making.
- BC Centre for Palliative Care: Serious Illness Conversation Guide
→ <http://www.bc-cpc.ca/cpc/>
- BC Guidelines: Palliative Care for the Patient with Incurable Cancer or Advanced Disease
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care>
- BC Palliative Care Benefits: Information for prescribers
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program>
- National Centre for Complementary and Alternative Medicine (NCCAM) for additional information on the use of non-pharmacological interventions
→ <https://nccih.nih.gov/>
- Canadian Association of Psychosocial Oncology: Pan-Canadian Practice Guideline: Screening, Assessment and Management of Psychosocial Distress, Depression and Anxiety in Adults with Cancer
→ http://www.capo.ca/wp-content/uploads/2015/11/FINAL_Distress_Guideline1.pdf
- Fraser Health psychosocial care guideline
→ <https://www.fraserhealth.ca/media/psychosocial%20care.pdf>

Resources specific to health organization/region

- Fraser Health
→ <http://www.fraserhealth.ca/health-professionals/professional-resources/hospice-palliative-care/>
- First Nations Health Authority
→ <http://www.fnha.ca/>

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- Interior Health
→ <https://www.interiorhealth.ca/YourCare/PalliativeCare/Pages/default.aspx>
- Island Health
→ http://www.viha.ca/pal_eol/
- Northern Health
→ <https://www.northernhealth.ca/Professionals/PalliativeCareEndofLifeCare.aspx>
- Providence Health
→ <http://hpc.providencehealthcare.org/>
- Vancouver Coastal Health
→ <http://www.vch.ca/your-care/home-community-care/care-options/hospice-palliative-care>

Resources specific to patient population

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians
→ <https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf>
- ALS Society of British Columbia 1-800-708-3228
→ www.alsbc.ca
- BC Cancer Agency: Symptom management guidelines
→ <http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management>
- BC Renal Agency: Conservative care pathway and symptom management
→ <http://www.bcrenalagency.ca/health-professionals/clinical-resources/palliative-care>
- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management
→ <http://www.bcheartfailure.ca/for-bc-healthcare-providers/end-of-life-tools/>
- Canuck Place Children's Hospice
→ <https://www.canuckplace.org/resources/for-health-professionals/>
 - 24 hr line – 1.877.882.2288
 - Page a Pediatric Palliative care physician – 1-604-875-2161 (request palliative physician on call)
- Together for short lives: Basic symptom control in pediatric palliative care
→ http://www.togetherforshortlives.org.uk/professionals/resources/2434_basic_symptom_control_in_paediatric_palliative_care_free_download

UNDERLYING CAUSES OF ANOREXIA IN PALLIATIVE CARE^{4, 11, 77, 90, 114}

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| 1. Primary | |
|---|--|
| <i>Metabolic disturbances</i> | |
| • Dehydration | • Uremia |
| • Hyperglycemia | • Hypothyroidism |
| • Hypokalemia hypercalcemia | • Cancer by-products (cytokines, tnf, interleukin 1, leptin) |
| <i>Inflammatory processes</i> | |
| • Hypercatabolism | • Cachexia |
| • Infection | |
| <i>Neuro-hormonal effects</i> | |
| • Gastric stasis | • Early satiety, anorexia, nausea, vomiting, constipation |
| • Malabsorption | |
| <i>Co-morbid conditions</i> | |
| • CHF | • Chronic renal failure |
| • COPD | • HIV/AIDS |
| <i>Concurrent disease</i> | |
| • Diabetes | • Anal fissure |
| • Hernia | • Anterior mucosal prolapse |
| • Diverticular disease | • Hemorrhoids |
| • Colitis | • Spinal cord injury |
| • Rectocele | • Multiple Sclerosis, ALS |
| <i>Neurological disorders</i> | |
| • Cerebral tumors | • Sacral nerve infiltration |
| • Autonomic failure | • Spinal cord involvement/compression |
| <i>Structural /Functional abnormalities</i> | |
| • GI obstruction | • Radiation fibrosis |
| • Dental problems | • Dysphagia (stroke, tumour, dementia) |
| 2. Secondary | |
| <i>Uncontrolled symptoms</i> | |
| • Pain | • Dyspnea |
| • Nausea/vomiting | • Altered taste/ xerostomia |
| • Constipation | • Treatment toxicities (mucositis) |
| <i>General</i> | |
| • Advanced age | • Decreased intake |
| • Inactivity | • Low fiber diet |
| • Need for assistance | • Delirium/dementia/memory problems |
| • Depression | • Poor fluid intake |
| • Sedation | • Physical or social impediments |
| • Pelvic tumor mass | • Painful anorectal conditions (anal fissure, hemorrhoids, perianal abscess) |

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| 3. Iatrogenic | |
|---------------------------|--|
| Drugs - drug classes | Specific causative examples* |
| • Antibiotics | Cefazolin, Dactinomycin, Doxycycline, Erythromycin, Metronidazole (1%), Nitrofurantoin, Rifampin, Sulfamethoxazole/Trimethoprim |
| • Anticonvulsants | Clobazam (up to 7%), Clonazepam, Divalproex Sodium (4 to 12%), Levetiracetam (3- 8%), Topiramate (10- 24%), Valproic acid (4- 12%) |
| • Antidepressants | Citalopram (4%), Bupropion (3 to 5%), Doxepin, Fluvoxamine (6%), Fluoxetine (3.8-17%), Nortriptyline, Paroxetine (2-9%), Sertraline (3-11%), Venlafaxine (8-22%) |
| • Antiretrovirals | Abacavir/Lamivudine/Zidovudine, Indinavir (0.5-5.4%), Nelfinavir (<2%), Tenofovir (3-4%) |
| • Antihypertensives | Amlodipine (0.1-1%), Clonidine, Hydralazine, Nadolol (<1%), Sotalol (1.6-2%) |
| • Antiparkinsonian agents | Bromocriptine, (4-5% in Acromegaly, type 2 diabetes), Levodopa/carbidopa (1.2%), Selegiline |
| • Antipsychotics | Haloperidol |
| • Antivirals | Acyclovir (<1%), Ganciclovir (15-19 %) |
| • Chemotherapy | Anastrozole (5-7%), Bevacizumab (34 to 43%), Busulfan(IV:85%), Capecitabine (9-26%), Cyclophosphamide, Cytarabine, Dacarbazine, Erlotinib (52%), Etoposide (10-13%), Fludarabine (0 up to 34%), Hydroxyurea, Letrozole (3-5%), Mitomycin (14%), Paclitaxel, Sorafenib (16-29%), Temozolomide (up to 40%), Vincristine |
| • Diuretics | Amiloride (3-8%), Ethacrynic acid, Furosemide, Hydrochlorothiazide (reported at doses of 25 mg or greater) |
| • Gastrointestinal agents | Aprepitant (5%-pediatric), Nabilone (8%) |
| • Hormonal agents | Flutamide (4%) |
| • Opioids | Fentanyl (Transdermal 3-10%, sublingual 1%), Hydro-morphone (1-6%), Morphine (5-10%), Tramadol (0.7-5.9 %) |
| • Other | Allopurinol, Amantadine (1-5%), Amiodarone (4-9%), Amphetamine (33%), Colestipol, Cyclobenzaprine (<1 %), Cyclosporine (2% or less), Dextroamphetamine, Donepezil (2-8%), Ethambutol, Famotidine, Flecainide (1-3%), Ketamine, Lithium, Memantine, Metformin, Methylphenidate (5%), Modafinil (4%), Pamidronate (1-12% in malignant hypercalcemia), Pancrelipase (6%), Polystyrene Sulfonate, Rivastigmine (1-6%), Sulfasalazine (33%), Trazodone (up to 3.5%), Zoledronic acid (hypercalcemia of malignancy, 9%; bone metastasis, 22%). |
| • Supplements | Folic acid, Iron (6%) |

If no specific percentage incidence shown for each drug, the known occurrence rate not reported.¹¹⁴ There are many medications that are reported to cause anorexia.¹¹⁴ This table above provides some examples. Consult pharmacist if additional assistance is required.

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| Drug, Action (classification) | Dose, Therapeutic Range | Onset, Adverse Effects, Precautions and Dosing Concerns |
|--|--|---|
| Dexamethasone[†] (corticosteroid) | <u>Starting dose:</u> 2 to 4 mg PO or IV/SC daily in AM <u>Maximum dose:</u> 4 to 8 mg PO or IV/SC daily in AM ^{77, 101} | Onset of appetite stimulation within a few days. ¹¹⁵ Adverse effects: candidiasis, fluid retention, gastritis, hypokalemia, hyperglycemia, myopathy, insomnia, impaired wound healing, psychosis. ^{14, 70, 105} After six weeks of use greater risk of steroid-induced diabetes, proximal myopathy, lipodystrophy (moon face, buffalo hump); after 3 months, of osteoporosis, glaucoma. ¹⁰⁵ For symptomatic gastroprotection while on corticosteroids, when if medical history suggests need, use a proton pump inhibitor such as pantoprazole or rabeprazole. Contraindicated when systemic infection, unless considered to be life-saving and specific anti-infective therapy is employed. ¹⁰⁵ Precautions: use in patients with psychotic illness (lower dose below 6 mg daily), seizure disorders, hypertension, diabetes. ⁷⁰ Dosing: most expert guidelines suggest up to a daily dose of 4 mg for anorexia with 8 mg daily dose typically only for anorexia with cachexia. ^{77, 101, 116} Assess for potential drug interactions, particularly anticoagulants, anticonvulsants and anticoagulants. Avoid NSAIDs, as increases peptic ulceration risk 15-fold together. ¹⁰⁵ Reduce dose to the minimum effective dose to avoid side effects. ¹¹⁵ |

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| Drug, Action (classification) | Dose, Therapeutic Range | Onset, Adverse Effects, Precautions and Dosing Concerns |
|---|--|--|
| Megestrol Acetate [†] (progesterone) | <u>Starting dose:</u> 160 mg PO daily <u>Maximum daily dose:</u> 800 mg daily ^{40, 117} | Onset of appetite stimulation may be up to 2 weeks. ¹¹⁵ Adverse effects: Edema, nausea, thromboembolic events, hypertension, breakthrough uterine bleeding, skin photosensitivity, insomnia, hypogonadism. ^{11, 115, 116} After 3 months of use, cushingoid changes and muscle catabolism. ⁹⁸ Megestrol may cause symptomatic suppression of the hypothalamic pituitary adrenal axis; in the presence of serious infection, surgery, or trauma, this complication may be life-threatening if not anticipated and treated. ⁹¹ Avoid during the first four months of pregnancy and while nursing infants. ^{118, 119} Precautions: use with caution if a history of thrombophlebitis in patients over 65 years of age who may have impaired renal function (as megestrol is substantially excreted via kidney). ^{118, 119} Monitor for possible adrenal cortical suppression if used continuously for prolonged periods. ^{118, 119} Dosing: 160 mg daily for anorexia. For <u>anorexia-cachexia in cancer patients</u> , optimal dose is 400 to 800 mg. ¹¹ Higher doses have no additional benefit. ¹¹⁶ Reduce dose gradually if used for more than 3 weeks to minimize risk of adrenal suppression. ^{14, 100} Liquid is indicated at 400 to 800 mg daily for the treatment of anorexia, cachexia, or an unexplained significant weight loss in patients with AIDS. ¹¹⁸ |
| Metoclopramide (prokinetic) | 5 to 10 mg PO TID to QID or IV/SC ¹⁴ | Can help early satiety, delayed gastric emptying, gastroparesis or nausea. Give 30 minutes prior to meals. ¹⁴ Adjust appropriately for reduced renal function, drug clearance. Metoclopramide itself has no appetite stimulating properties. ^{101, 111} Not shown to improve caloric intake. ⁹¹ |
| Domperidone (prokinetic) | 10 mg PO TID to QID | Can help early satiety, delayed gastric emptying, gastroparesis or nausea. Give 30 minutes prior to meals. ¹⁴ Adjust appropriately for reduced renal function, drug clearance. Prokinetics not shown to directly stimulating appetite. |

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| Drug, Action (classification) | Dose, Therapeutic Range | Onset, Adverse Effects, Precautions and Dosing Concerns |
|--|--|---|
| Mirtazapine (antidepressant) | 7.5 to 30 mg PO daily at bedtime ^{5, 120} | Adjust appropriately for reduced renal function, drug clearance. Well tolerated, ^{120, 121} causes sedation (give dose at bedtime) Use for anorexia is an off-label indication. When studied for anorexia, dose increased after 3 to 7 days, patients responded in the first few weeks. ¹²¹ |
| Nystatin (antifungal) | 5 mL PO QID x 14 days | For treatment of oral candidiasis. Swish and swallow. Avoid food and water for a while after dose is given to improve contact effectiveness. |

†Off-label. PO = by mouth IV = Intravenous, SC = Subcutaneous, TID = three times daily, QID = four times daily, ODT = oral dissolving tablet, CSCI = continuous subcutaneous infusion.

Prices for prescription drugs may be obtained from BC PharmaCare. The British Columbia Palliative Care Benefits Plan (<http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/palliative-formulary.pdf>) provides province wide drug coverage for many of the recommended medications— check website to confirm coverage. **Consider price when choosing similarly beneficial medications, especially when the patient / family is covering the cost.**

ANOREXIA MANAGEMENT ALGORITHM

No management algorithm included in this document.

ANOREXIA EXTRA RESOURCES OR ASSESSMENT TOOLS

No extra resources or assessment tools Included in this document.

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DEFINITION

Dehydration is intracellular water depletion with hypernatremia (hyperosmolality); it usually presents with symptoms of thirst, anorexia, nausea/vomiting, fatigue and irritability. Physical findings may include lethargy, confusion, muscle twitching and hyperreflexia. **Volume depletion** is the loss of intravascular water (with varying sodium levels) and presents with diminished skin turgor/capillary refill and orthostatic hypotension and dizziness.¹ **Artificial hydration** (AH) involves the provision of water or electrolyte solutions by any route other than the mouth. This can be achieved by intravenous, subcutaneous (hypodermoclysis)² and dermal (dermoclysis).³ **Overhydration** related symptoms include: bronchial secretions, respiratory congestion, pleural effusion, nausea/vomiting, ascites, peripheral edema.⁴

PREVALENCE

In older adults, dehydration is one of the 10 most frequent diagnoses for hospitalization. In frail elderly people, it is the most common fluid and electrolyte disorder.⁵ In one study of palliative patients with cancer diagnosis, hypernatremia was present in 55% of clients; hypercalcemia was present in 23%.⁶

IMPACT

In the clinical setting, it is not uncommon for distressed patients who are unable to eat or drink (and their families) to emotionally plead with healthcare providers to intervene.^{7,8} When patients with a life-limiting illness are unable to adequately take in nutrition and fluids, the issue of perceived starvation and eventual death rises to the forefront, resulting in stress on both health providers and families. Dehydration causes few symptoms for patients who are comatose and comfortable, but can contribute to a delirium.⁹ During the dying process, patients may have diminished awareness, which may decrease their perception of thirst and hunger as they naturally progress toward coma and death.³

STANDARD OF CARE

Step 1 | Goals of care conversation

Determine goals of care in conversation with the patient, family and inter-disciplinary team. Refer to additional resources ([Additional resources for management of dehydration](#)) for tools to guide conversations and required documentation. Goals of care may change over time and need to be reconsidered at times of transition, e.g., disease progression or transfer to another care setting.

Step 2 | Assessment

Dehydration Assessment: Using Mnemonic O, P, Q, R, S, T, U and V²²

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| Mnemonic Letter | Assessment Questions <i>Whenever possible, ask the patient directly. Involve family as appropriate and desired by the patient.</i> |
|-------------------------------|---|
| O nset | When did you start to feel dehydrated? Have you experienced it before? How long does it last? How often does it occur? |
| P rovoking /Palliating | What brings it on? What makes it better? What makes it worse? |
| Q uality | What does it feel like (dry mouth / skin, thirst)? Can you describe it? |
| R egion/Radiation | Not applicable |
| S everity | How severe is this symptom? What would you rate it on a scale of 0-10 (0 being none and 10 being the worst possible)? Right now? At worst? On average? How bothered are you by this symptom? Are there any other symptom(s) that accompany this symptom? |
| T reatment | What medications and treatments are you currently using? Are you using any non-prescription treatments, herbal remedies, or traditional healing practices? How effective are these? Do you have any side effects from the medications and treatments? What have you tried in the past? Do you have concerns about side effects or cost of treatments? |
| U nderstanding | What do you believe is causing this symptom? How is it affecting you and/or your family? What is most concerning to you? |
| V alues | What overall goals do we need to keep in mind as we manage this symptom? What is your acceptable level for this symptom (0-10)? Are there any beliefs, views or feelings about this symptom that are important to you and your family? |

Symptom Assessment: Physical assessment as appropriate for symptom

It is often difficult to assess hydration in people with advanced illness; therefore, findings from a variety of observations and assessments are most reliable.¹⁰ **History** – assess appetite, oral intake, associated symptoms (e.g., nausea, vomiting, diarrhea, drowsiness, fatigue, and confusion). **Physical Examination** – assess skin and oral cavity, dry mucous membranes, jugular venous pressure, blood pressure, pulse, temperature, ascites, muscle weakness. Urine may be darker in colour due to dehydration or other factors, such as jaundice.

Note: In severe cachexia, the skin turgor is hard to assess and is often not reliable. Similarly, thirst and edema are not good indicators of hydration status.¹⁰

Diagnostics: consider goals of care before ordering diagnostic testing

- May include serum urea, creatinine, sodium, hematocrit, albumin and glucose.

Step 3 | Determine possible causes and reverse as possible if in keeping with goals of care

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Fluid deficits in terminally ill patients are frequently multifactorial. Regardless of the cause, the end result is total body water depletion and decreased renal function. There are 2 broad categories of fluid deficit disorders which may present separately or together:

- **Dehydration**, which results from total body water depletion.
- **Hypovolemia or volume depletion**, which results from loss of both salt and water, mainly from the extracellular (intravascular) space.³

PRINCIPLES OF MANAGEMENT



When considering a management approach, always balance burden of a possible intervention against the likely benefit (e.g., does the intervention require transfer to another care setting?)

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- Capable adults have the right to decide for themselves whether to stop eating and drinking and whether or not they would like to withdraw or withhold artificial nutrition and hydration.
- Decisions for patients who lack decision-making capacity should be made in accordance with advance directives and/or persons legally designated by the patient or the Temporary Substitute Decision Maker.³
- If the effort to eat and drink becomes too burdensome or is not welcome, the patient should not be pressured to make this effort.³
- Dehydration in dying persons is associated with some benefits: reduced urine output with reduced need to void or use catheters; less gastrointestinal fluid with decreased frequency and severity of edema and ascites; may act as a natural anesthetic for the central nervous system.⁸
- When deciding to initiate or stop hydration, discuss goals of care, risks and benefits along with the patient's preferences.¹
- In case of uncertainty of the benefits and risks of parenteral hydration in a particular patient, a brief trial with clearly defined goals may be appropriate to initiate, followed by re-assessments of its clinical benefits and harm.⁷

Step 4 | Interventions

LEGEND FOR USE OF BULLETS

Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence, using a modified GRADE process.

| | |
|--|--|
|  | Use with confidence: recommendations are supported by moderate to high levels of empirical evidence. |
|  | Use if benefits outweigh potential harm: recommendations are supported by clinical practice experience, anecdotal, observational or case study evidence providing low level empirical evidence. |
|  | Use with caution: Evidence for recommendations is conflicting or insufficient, requiring further study |
|  | Not recommended: high level empirical evidence of no benefit or potential harm |

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Interventions available in the home and residential care facilities

-  **Oral intake** is the preferred route as long as it is well tolerated. Popsicles, frozen yogurt, ice chips made from water or fruit juice, and commercial instant breakfast drinks or milkshakes can be offered. Bendable straws and sports bottles can be helpful.¹⁰
-  Dry mouth can be treated with an intensive, every-2-hour **schedule of mouth care**, including hygiene, lip lubrication, artificial saliva and ice chips.³

Interventions requiring additional equipment or admission to acute care

Artificial hydration (AH) - see [Dyhydration extra resources or assessment tools for burdens and benefits](#)

-  Research does not support that parenteral hydration improves signs of dehydration, survival or quality of life; in temporary, short-term situations, it may alleviate symptoms related to dehydration and decreased mental cognition.¹
-  Mixed evidence to support hydration and possible opioid rotation to improve delirium symptoms related to opioid toxicity.
-  Parenteral AH can be administered through hypodermoclysis (fluid infused into the subcutaneous tissue) or Intravenous. Hypodermoclysis lacks firm evidence of benefit. Trial only for symptomatic dehydration.¹⁵ Refer to your local policies and pre-printed orders if trialing hypodermoclysis.

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Questions re AH decisions include

- Will it prolong survival?
- Will it alleviate symptoms? Improve quality of life?
- If so, what method of AH is best?¹⁴
- What are the implications for the patient remaining in their place of choice?

Refer to [Dyhydration extra resources or assessment tools](#) for further decision support.

Pharmacological interventions

-  **Reduce or remove any drugs, if possible, that may cause or contribute to dehydration** such as diuretics, alcohol, excessive laxative use or lithium which also pose a risk.^{16,17}
-  **Consider consultation with a pharmacist** when drug-related dehydration problems are suspected such as: Dry mouth (antidepressants, antihistamines, anticholinergics), reduced thirst sensation (antipsychotics), greater sweating (venlafaxine, opioids), or sedation and reduction in judgement (benzodiazepines).^{1,17}
-  **Assess risk of drug toxicity** due to fluid loss, or if renal function reduces elimination of drugs or their metabolites.³
-  Adjust dose to accommodate reduced drug clearance, discontinue/taper drugs or switch to drugs more suitable for poorer renal function.
-  If reduced renal function review analgesics, psychoactive drugs, antibiotics, metoclopramide, gabapentin, digoxin, ACE inhibitors, and others.
-  Opioids such as morphine and its metabolite, codeine, should be avoided in presence of kidney disease as they risk inducing toxicity appearing as myoclonus.¹⁸
-  There is mixed evidence supporting hydration and possible opioid rotation to improve myoclonus or delirium symptoms related to opioid toxicity.^{1,18}
-  **Monitor patient performance status in dysphagia** as medication routes capacity; routes and options may be actively changing when dehydration exists.
-  **Update drug management** to best control new or existing symptoms according to goals of care including:
 -  Delirium, sedation, cognition – often distressing to families.^{1,3}
 -  Nausea, fatigue, anorexia, dry mouth and thirst – as may occur often.
 -  Hypotension, dizziness, diarrhea, sweating, constipation, fever (including neoplastic), infection, respiratory congestion, neuromuscular irritability, diabetes, heat-related illness.¹⁹
 -  Overhydration contributes to edema, ascites, respiratory congestion.
 -  Electrolyte management.

Utilize other symptom guidelines and seek consultation with interdisciplinary professionals as appropriate.

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-  Families need explanation, support and recognition that this is a difficult transition.⁹
-  Communicate clearly with patients and family about the limited evidence of beneficial effects of AH.¹
-  Help the family to understand that artificial hydration is often not indicated when the patient is dying and will not improve the patient's condition.³
-  Explain that the body no longer needs large amounts of energy and the patient's digestive system is progressively slowing down.¹² Help the patient and family understand that the loss of appetite and reduced fluid intake is a normal part of the dying process.
-  Explain that attempts to counteract this process could create unpleasant symptoms from fluid the body cannot process such as bloating, swelling, cramps, diarrhea, and shortness of breath, without improving the outcome.¹³
-  Encourage the family to do mouth care, if appropriate, as a way to contribute to their loved one's comfort.

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Resources specific to dehydration

- BC Cancer Agency: Xerostomia
→ <http://www.bccancer.bc.ca/nursing-site/Documents/18.%20Xerostomia.pdf>

General Resources

- **Provincial Palliative Care Line** – for **physician** advice or support, call **1 877 711-5757** In ongoing partnership with the Doctors of BC, the toll-free Provincial Palliative Care Consultation Phone Line is staffed by Vancouver Home Hospice Palliative Care physicians 24 hours per day, 7 days per week to assist physicians in B.C. with advice about symptom management, psychosocial issues, or difficult end-of-life decision making.
- BC Centre for Palliative Care: Serious Illness Conversation Guide
→ <http://www.bc-cpc.ca/cpc/>
- BC Guidelines: Palliative Care for the Patient with Incurable Cancer or Advanced Disease
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care>
- BC Palliative Care Benefits: Information for prescribers
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program>
- National Centre for Complementary and Alternative Medicine (NCCAM) for additional information on the use of non-pharmacological interventions
→ <https://nccih.nih.gov/>
- Canadian Association of Psychosocial Oncology: Pan-Canadian Practice Guideline: Screening, Assessment and Management of Psychosocial Distress, Depression and Anxiety in Adults with Cancer
→ http://www.capo.ca/wp-content/uploads/2015/11/FINAL_Distress_Guideline1.pdf
- Fraser Health psychosocial care guideline
→ <https://www.fraserhealth.ca/media/psychosocial%20care.pdf>

Resources specific to health organization/region

- Fraser Health
→ <http://www.fraserhealth.ca/health-professionals/professional-resources/hospice-palliative-care/>
- First Nations Health Authority
→ <http://www.fnha.ca/>
- Interior Health
→ <https://www.interiorhealth.ca/YourCare/PalliativeCare/Pages/default.aspx>

Additional resources for management of dehydration continued on [next page](#)

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- Island Health
→ http://www.viha.ca/pal_eol/
- Northern Health
→ <https://www.northernhealth.ca/Professionals/PalliativeCareEndofLifeCare.aspx>
- Providence Health
→ <http://hpc.providencehealthcare.org/>
- Vancouver Coastal Health
→ <http://www.vch.ca/your-care/home-community-care/care-options/hospice-palliative-care>

Resources specific to patient population

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians
→ <https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf>
- ALS Society of British Columbia 1-800-708-3228
→ www.alsbc.ca
- BC Cancer Agency: Symptom management guidelines
→ <http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management>
- BC Renal Agency: Conservative care pathway and symptom management
→ <http://www.bcrenalagency.ca/health-professionals/clinical-resources/palliative-care>
- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management
→ <http://www.bcheartfailure.ca/for-bc-healthcare-providers/end-of-life-tools/>
- Canuck Place Children's Hospice
→ <https://www.canuckplace.org/resources/for-health-professionals/>
 - 24 hr line – 1.877.882.2288
 - Page a Pediatric Palliative care physician – 1-604-875-2161 (request palliative physician on call)
- Together for short lives: Basic symptom control in pediatric palliative care
→ http://www.togetherforshortlives.org.uk/professionals/resources/2434_basic_symptom_control_in_paediatric_palliative_care_free_download

UNDERLYING CAUSES OF DEHYDRATION IN PALLIATIVE CARE

Information is included in the body of this document

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MEDICATIONS FOR MANAGEMENT OF DEHYDRATION

Medication information is included in the body of this document

Prices for prescription drugs may be obtained from BC PharmaCare. The British Columbia Palliative Care Benefits Plan <http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/palliative-formulary.pdf> provides province wide drug coverage for many of the recommended medications—check website to confirm coverage. **Consider price when choosing similarly beneficial medications, especially when the patient / family is covering the cost.**

DEHYDRATION MANAGEMENT ALGORITHM

No management algorithm included in this document

DEHYDRATION EXTRA RESOURCES OR ASSESSMENT TOOLS

Artificial hydration (IV/SC fluids) during the dying phase: to use or not to use?^{1,4,7,8,20, 21}

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| Global Benefits of Artificial hydration (AH) | Global Burdens of Artificial Hydration (AH) |
|--|---|
| No strong evidence exists supporting the use of parenteral hydration for the majority of terminally ill patients; however, a subset of patients may derive some benefit. ⁷ | |
| May improve: <ul style="list-style-type: none"> • Circulation of drugs to relieve symptoms. • Skin turgor and reduce pressure sores (or not) • Alertness and fatigue. | May make death less 'natural', i.e., medicalized. Family may be less able to cuddle and get close with the pump/drip stand. Family may feel inhibited re closeness due to equipment. |
| May improve cognitive function if related to terminal agitation secondary to neurotoxicity. May prolong survival in specific, reversible causes such as hypercalcemia or opioid neurotoxicity. | May cause iatrogenic overhydration, leading to exacerbation of physical symptoms such as: pulmonary edema, ascites, vomiting, peripheral edema, respiratory congestion, restlessness from full bladder. |
| May reduce thirst in some patients (note: good mouth care usually does as good a job). Focus on managing dry mouth. | May deter patients from being at home. |
| Seems less like care providers are just letting the patient die (but remember, he or she is dying from the disease, not dehydration). Ask: who are we treating really—us, the relatives, or the patient? | Infusion set getting in the way of human touch. May encumber the patient's movement, mobility and closeness. |
| Specific to hypodermoclysis – subcutaneous (S/C) delivery | |
| S/C usage may avoid need for IV insertion or transfers to acute care setting. Can sometimes be administered in the home or residential care settings. | IV tubing, bags, fluid and S/C needles required. |
| No venipuncture skills required | |
| May enhance effectiveness of pain medication. | Potential for overhydration remains. |
| Can be administered slowly overnight; can administer low fluid volumes. Lower potential for iatrogenic overhydration than with IV hydration. | Not all residential care settings or community care services have capacity to administer. |

Dehydration extra resources or assessment tools continued on [next page](#)

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| Specific to Intravenous delivery | |
|--|--|
| May improve clinical conditions secondary to medication toxicities. | Venipuncture skills and equipment required. IV catheters/needles are painful and infusion sets are constraining. IVs are invasive and intrusive and can contribute to patient and family discomfort. |
| Can be administered in acute care and ER settings. | Transfer to acute care or ER may cause patient distress, discomfort and disruption to personal goals and wishes. |
| Most rapid response to dehydration: monitor closely. | May cause iatrogenic overhydration leading to exacerbation of physical symptoms such as: pulmonary edema, ascites, vomiting, peripheral edema, respiratory congestion, restlessness from full bladder. |
| While relatively large hydration volumes can worsen or lead to pleural effusion and/or excess bronchial secretions, low volumes (<1000 mL daily) appear to be safely tolerated. ³ | |

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RESPIRATORY CONGESTION

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DEFINITION

Respiratory congestion -- also called ‘noisy respirations’, ‘noisy breathing’, ‘respiratory tract secretions’ (RTS) and ‘death rattle’ -- is the noise produced by the turbulent movements of secretions in the upper airways that occur during respiration in patients who are dying.¹ This guideline does not support the term ‘death rattle’, especially with families, encouraging instead use of term **respiratory congestion**. It may be classified as either Type 1 or Type 2:

Type 1: The noise that ensues when excessive secretions are produced by the salivary glands when the patient is unable to swallow due to reduced level of consciousness or profound weakness. Is reported to predict death for 75% of dying patients, often within 48 hours of onset.^{1,2}

Type 2: The presence of mostly bronchial secretions caused by respiratory pathology such as pulmonary infection, aspiration, and/or edema. Type 2 is much more difficult to treat and may be unaffected by standard palliation treatment.³

PREVALENCE

Respiratory congestion in the dying patient is a common and expected symptom⁴ although reported prevalence varies considerably, from 23-92%.^{5,6} Respiratory congestion may cluster alongside dyspnea; see dyspnea guidelines for management.

IMPACT

If the person is alert, respiratory secretions can cause him or her to feel agitated and fearful of suffocating.¹ Family may interpret the sound as an indication that the patient is ‘drowning in secretions’ so it is not surprising that it has been reported as upsetting at the time of dying and even several years after the death.² Some professionals may also find the sound distressing.⁵ **However, there is no evidence that the sound is associated with respiratory distress.**⁴

STANDARD OF CARE

Step 1 | Goals of care conversation

Determine goals of care in conversation with the patient, family and inter-disciplinary team. Refer to additional resources ([Additional resources for management of respiratory congestion](#)) for tools to guide conversations and required documentation. Goals of care may change over time and need to be reconsidered at times of transition, e.g., disease progression or transfer to another care setting.

Step 2 | Assessment

Respiratory congestion assessment: Using Mnemonic O, P, Q, R, S, T, U and V ^{5,7, 32}

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| Mnemonic Letter | Assessment Questions <i>Whenever possible, ask the patient directly. Involve family as appropriate and desired by the patient. At the onset of congestion, most patients are at a reduced consciousness level⁸; therefore, assessment is usually dependent on family or care provider observations.</i> |
|-------------------------------|--|
| O nsset | When did it begin? How long does it last? How often does it occur? |
| P rovoking /Palliating | What brings it on? What makes it better? What makes it worse? Can the secretions be cleared by coughing or swallowing? |
| Q uality | What does it sound like? Can you describe it? |
| R egion/Radiation | Does it seem to be in the chest? Or throat? |
| S everity | Does the patient appear comfortable? Are the sounds louder or quieter with change of positions? ⁷ How bothered are you by this symptom? Are there any other symptom(s) that accompany this symptom? |
| T reatment | What medications and treatments are you currently using? Are you using any non-prescription treatments, herbal remedies, or traditional healing practices? How effective are these? Do you have any side effects from the medications and treatments? What have you tried in the past? Do you have concerns about side effects or cost of treatments? Could other treatments be worsening this symptom (e.g., artificial hydration)? |
| U nderstanding | What do you believe is causing this symptom? How is it affecting you and/or your family? What is most concerning to you? Does the patient appear distressed? ⁷ |
| V alues | What overall goals do we need to keep in mind as we manage this symptom? Are there any beliefs, views or feelings about this symptom that are important to you and your family? |

Symptom Assessment: Physical assessment as appropriate for symptom

Diagnostics: consider goals of care before ordering diagnostic testing

Step 3 | Determine possible causes and reverse as possible if in keeping with goals of care

- The cause of noisy breathing remains unproven but is presumed to be due to an accumulation of secretions in the airways.⁶
- Factors associated with an increased risk, particularly of Type 2, include: a prolonged dying phase, cerebral or pulmonary malignancy, pneumonia, dysphagia, and head injury.^{1, 2, 9}
- Excessive oropharyngeal secretions, coupled with a weakening gag and/or cough reflex, cause pooling of the secretions and saliva.¹⁰

PRINCIPLES OF MANAGEMENT



When considering a management approach, always balance burden of a possible intervention against the likely benefit (e.g., does the intervention require transfer to another care setting?)

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- Although the sound of respiratory congestion can be disturbing to hear, determine if the patient is distressed by observing other indicators (such as wincing) and reassure family.
- If the patient seems distressed, start medication early for best effect.
- Positioning is the most effective non-pharmacological intervention.
- Suctioning may cause more harm and not relieve the congestion

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LEGEND FOR USE OF BULLETS

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Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence, using a modified GRADE process.

| | |
|--|--|
|  | Use with confidence: recommendations are supported by moderate to high levels of empirical evidence. |
|  | Use if benefits outweigh potential harm: recommendations are supported by clinical practice experience, anecdotal, observational or case study evidence providing low level empirical evidence. |
|  | Use with caution: Evidence for recommendations is conflicting or insufficient, requiring further study |
|  | Not recommended: high level empirical evidence of no benefit or potential harm |

Non-pharmacological interventions

Interventions available in the home and residential care facilities

-  **Limit or discontinue use** of IV fluids or artificial nutrition to decrease burden of secretions.^{1, 10, 11.}
-  **Sips of fluids only** if patient is alert and able to swallow.
-  Provide **frequent mouth care; humidify room** (fill a bathtub with water, keep plants, use a humidifier machine if available).¹⁰
-  **Reposition** the patient in a side-lying position with the head of the bed elevated.
-  **Position** onto alternate side to encourage postural drainage.²

Interventions requiring additional equipment or admission to acute care

-  **Avoid suction** when possible. It can cause agitation and distress, is ineffective below the oropharynx, and does not correct underlying problem.^{1, 11.}
-  In the event of copious secretions in the oropharynx, gentle anterior suction may be useful.^{3, 5, 12} **However, consider goals of care, equipment availability, and your organization's policies.**
-  Patients with a tracheotomy who have previously required suction as part of their ongoing management, may continue to require it.
-  With active bleeding from oral, esophageal or pulmonary areas, suction may be required (see severe bleeding guideline).

Pharmacological interventions

Evidence of superiority not established for any specific medication or benefit over placebo.^{5, 6, 14, 15.}

-  Use of anticholinergic drugs remains high in clinical practice, up to 80-88%,^{8, 16} despite the lack of evidence.^{8, 17} They are also recommended in the UK national guidelines.¹⁸ Routine or standard use of anticholinergics has been increasingly questioned.^{4, 5, 18, 19}
-  When drugs are used, combine with non-pharmacological interventions. (See non-pharmacological interventions section.²⁰)

In BC, drug choices used are primarily either glycopyrrolate, atropine or scopolamine.

Starting therapy (for further drug dosing and precautions, see [Medications for management of respiratory congestion](#)):

-  When started, begin at the first audible sign of congestion, as drugs do not dry up secretions that are already present.⁷
-  Anticholinergics may be more effective when started early, or in patients with a lower intensity of congestion.^{8, 21, 22}
-  Onset of effect for subcutaneous route reported within 30 to 60 minutes from anticholinergics.²¹

Alternative routes

-  Subcutaneous administration of anticholinergics is most commonly used; however, consider alternative routes in the community due to the need for equipment and training for administration.
-  Other routes of administration include transdermal (scopolamine patch) or sublingual (atropine 1% ophthalmic drops). The use of atropine sublingually, 1 to 3 drops every two to four hours, has been suggested while patients are starting on scopolamine patch as patch can take 6 to 8 hours to be effective; steady state levels reached in 24 hours.²³

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Monitoring of beneficial effects and undesirable adverse effects

-  Oropharyngeal secretions (Type 1 respiratory congestion) is most likely to respond to drug therapy, while treatment success for bronchial secretions (Type 2) is poor, if at all.^{20, 24}
-  Common adverse effects are dry mouth, urinary retention, visual disturbances and occasionally confusion.^{6, 18} A significant difference in the incidence of adverse effects amongst each of the anticholinergics has not been established.²¹ Provide good mouth care and lubricate eyes with drops if necessary as mucous membranes often become dry.
-  Patients are commonly unable to report benefit or adverse effects due to reduced level of consciousness.⁸
-  Consider stopping anticholinergics if congestion is not helped. Often treatment may be initiated for the benefit of relatives and others.^{6, 25} Do not continue use merely as a drive to “do something” if ineffective or if distress levels are unaltered.²⁶ Monitor symptoms regularly after drug discontinuation.
-  Octreotide had no anti-secretory benefit on respiratory congestion intensity when compared with scopolamine in a 10-patient randomized trial.²⁷ Higher cost precludes use.
-  Although perceived benefit of oxygen administration or measurement of oxygen saturation remains high at 83%, oxygen has no known patient benefit for respiratory congestion.¹³

Patient and family education

-  Use plain language such as ‘moist or noisy breathing’. Avoid the term ‘death rattle’ when talking with families or other clinicians.¹
-  Inform families in advance that noisy breathing may occur as a normal part of the dying process.^{2, 9-11}
-  Inform families that oxygen does not change the noisy breathing and is not beneficial.¹³ If in community, a family decision to seek oxygen may lead to unnecessary emergency department visits.
-  Family distress with noisy breathing decreases when they see patient is comfortable.⁵ Point out non-verbal indicators of comfort such as facial expression. If the patient appears comfortable, reassure the family; if patient has laboured breathing or appears uncomfortable, treat the dyspnea and/or pain.¹¹
-  If appropriate, encourage family involvement in providing mouth care as a way to care for their loved one.

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Resources Specific to Respiratory Congestion

- ALS Society of Canada: A guide to ALS patient care for primary care physicians. Sections on sialorrhea (drooling due to decreased ability to manage saliva), dyspnea and palliative care
→ <https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf>

General Resources

- **Provincial Palliative Care Line** – for **physician** advice or support, call **1 877 711-5757** In ongoing partnership with the Doctors of BC, the toll-free Provincial Palliative Care Consultation Phone Line is staffed by Vancouver Home Hospice Palliative Care physicians 24 hours per day, 7 days per week to assist physicians in B.C. with advice about symptom management, psychosocial issues, or difficult end-of-life decision making.
- BC Centre for Palliative Care: Serious Illness Conversation Guide
→ <http://www.bc-cpc.ca/cpc/>
- BC Guidelines: Palliative Care for the Patient with Incurable Cancer or Advanced Disease
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care>
- BC Palliative Care Benefits: Information for prescribers
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program>
- National Centre for Complementary and Alternative Medicine (NCCAM) for additional information on the use of non-pharmacological interventions
→ <https://nccih.nih.gov/>
- Canadian Association of Psychosocial Oncology: Pan-Canadian Practice Guideline: Screening, Assessment and Management of Psychosocial Distress, Depression and Anxiety in Adults with Cancer
→ http://www.capo.ca/wp-content/uploads/2015/11/FINAL_Distress_Guideline1.pdf
- Fraser Health psychosocial care guideline
→ <https://www.fraserhealth.ca/media/psychosocial%20care.pdf>

Resources specific to health organization/region

- Fraser Health
→ <http://www.fraserhealth.ca/health-professionals/professional-resources/hospice-palliative-care/>
- First Nations Health Authority
→ <http://www.fnha.ca/>
- Interior Health
→ <https://www.interiorhealth.ca/YourCare/PalliativeCare/Pages/default.aspx>

Additional resources for management of respiratory congestion continued on [next page](#)

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- Island Health
→ http://www.viha.ca/pal_eol/
- Northern Health
→ <https://www.northernhealth.ca/Professionals/PalliativeCareEndofLifeCare.aspx>
- Providence Health
→ <http://hpc.providencehealthcare.org/>
- Vancouver Coastal Health
→ <http://www.vch.ca/your-care/home-community-care/care-options/hospice-palliative-care>

Resources specific to patient population

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians
→ <https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf>
- ALS Society of British Columbia 1-800-708-3228
→ www.alsbc.ca
- BC Cancer Agency: Symptom management guidelines
→ <http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management>
- BC Renal Agency: Conservative care pathway and symptom management
→ <http://www.bcrenalagency.ca/health-professionals/clinical-resources/palliative-care>
- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management
→ <http://www.bcheartfailure.ca/for-bc-healthcare-providers/end-of-life-tools/>
- Canuck Place Children's Hospice
→ <https://www.canuckplace.org/resources/for-health-professionals/>
 - 24 hr line – 1.877.882.2288
 - Page a Pediatric Palliative care physician – 1-604-875-2161 (request palliative physician on call)
- Together for short lives: Basic symptom control in pediatric palliative care
→ http://www.togetherforshortlives.org.uk/professionals/resources/2434_basic_symptom_control_in_paediatric_palliative_care_free_download

UNDERLYING CAUSES OF RESPIRATORY CONGESTION IN PALLIATIVE CARE

Information is included in the body of the document.

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| Subcutaneous Drug | Stat and PRN Subcutaneous dose | CSCI dose per 24 hours | Adverse effects information | Precautions |
|---|---------------------------------------|------------------------|--|--|
| Glycopyrrolate | 0.2 mg-0.4mg Q4-6H | 0.6 to 1.2 mg | Does not cross BBB. CNS adverse effects may be minimized | Half dose in end-stage renal failure |
| Atropine | 0.4 to 0.6 mg Q4-6H | 1.2 to 2 mg | May be stimulating, rather than sedating. Use IV may have risk of tachycardia. | Cardiac effects, at higher doses. |
| Scopolamine (hyoscine HYDRObromide) | 0.4 mg to 0.6mg Q4-6H | 1.2 to 2 mg | May be more sedating | Avoid in end-stage renal failure due to increased risk of delirium |
| Hyoscine BUTYLbromide (e.g. Buscopan) | 20 mg Repeat doses every 4 to 6 hours | 20 to 120 mg | Does not cross BBB. CNS adverse effects may be minimized | Use may be confused with scopolamine due to similar name. Use TALLman lettering to differentiate. |
| Transdermal and Sublingual Drugs | | | | |
| Scopolamine Transdermal Apply one patch every 72 hours (allow for 6-8 hrs onset of action, steady levels at 24 hrs) Each 1.5 mg patch release approximately 1 mg of scopolamine base over 72 hours. Multiple (e.g. two) concurrent patches have been used. | | | | Locate behind ear(s) for optimal absorption. |
| Atropine 1% ophthalmic drops for SUBLINGUAL use 1 to 4 drops (providing approximately 0.5 mg per drop) sublingual every two to four hours. | | | | Avoid inadvertent and unintended administration into eyes. Effectiveness not established. Off-label indication |

† Off-label. PO = by mouth IV = Intravenous, SC = Subcutaneous, TID = three times daily, QID = four times daily ODT = oral dissolving tablet CSCI = continuous subcutaneous infusion.

Prices for prescription drugs may be obtained from BC PharmaCare. The British Columbia Palliative Care Benefits Plan <http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/palliative-formulary.pdf> provides province wide drug coverage for many of the recommended medications— check website to confirm coverage. **Consider price when choosing similarly beneficial medications, especially when the patient / family is covering the cost.**

RESPIRATORY CONGESTION MANAGEMENT ALGORITHM

No management algorithm included in this document.

RESPIRATORY CONGESTION EXTRA RESOURCES OR ASSESSMENT TOOLS

No extra resources or assessment tools included in this document.

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1. Dudgeon D. Dyspnea, Death Rattle and Cough. 2016. In: Care of the Imminently Dying [Internet]. Oxford Medicine Online: Oxford University Press; [1-15].
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DYSPNEA

DEFINITION

Dyspnea is the uncomfortable feeling of being short of breath. It may or may not be associated with hypoxia.

PREVALENCE

Prevalence is high in palliative patients, e.g., in cancer (10-70%), COPD (90-95%), and CHF (60-88%).¹ Intensity tends to worsen towards end of life.²

IMPACT

Results in multidimensional distress to patients and caregivers.³ Quality of life and daily functions can be profoundly negatively impacted. Psychological effects include: anxiety, panic, hopelessness, loss of enjoyment of life, and social isolation.^{1,4} Survival may be shortened in dyspnea patients, averaging as little as 30 days.⁵

STANDARD OF CARE

Step 1 | Goals of care conversation

Determine goals of care in conversation with the patient, family and inter-disciplinary team. Refer to additional resources ([Additional resources for management of dyspnea](#)) for tools to guide conversations and required documentation. Goals of care may change over time and need to be reconsidered at times of transition, e.g., disease progression or transfer to another care setting.

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Step 2 | Assessment

Dyspnea Assessment: Using Mnemonic O, P, Q, R, S, T, U and V⁴⁷

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| Mnemonic Letter | Assessment Questions <i>Whenever possible, ask the patient directly. Involve family as appropriate and desired by the patient.</i> |
|-------------------------------|---|
| O nset | When did it begin? How long does it last? How often does it occur? |
| P rovoking /Palliating | What brings it on? What makes it better? What makes it worse? |
| Q uality | What does it feel like? Can you describe it? Is it worse lying down or sitting? |
| R egion/Radiation | Not applicable. |
| S everity | How severe is this symptom? What would you rate it on a scale of 0-10 (0 being none and 10 being the worst possible)? Right now? At worst? On average? When you are walking? Or climbing stairs? Or doing activities of daily living? ¹ How bothered are you by this symptom? Are there any other symptom(s) that accompany this symptom (e.g., pain in your chest, anxiety, fatigue)? |
| T reatment | What medications and treatments are you currently using? Are you using any non-prescription treatments, herbal remedies, or traditional healing practices? How effective are these? Do you have any side effects from the medications and treatments? What have you tried in the past? Do you have concerns about side effects or cost of treatments? |
| U nderstanding | What do you believe is causing this symptom? How is it affecting you and/or your family? What is most concerning to you? |
| V alues | What overall goals do we need to keep in mind as we manage this symptom? What is your acceptable level for this symptom (0-10)? Are there any beliefs, views or feelings about this symptom that are important to you and your family? What are you having trouble doing because of this symptom that you would like to do? |

Symptom Assessment: Physical assessment as appropriate for symptom

Diagnostics: consider goals of care before ordering diagnostic testing

- If indicated, complete: blood count, electrolytes, renal function, oxygen saturation by oximetry, and chest x-ray.
- The choice of appropriate diagnostic tests should be guided by the stage of disease, the prognosis, the balance of the benefits and burdens, treatment goals, and patient preferences. Tests are exhausting for people in a palliative care setting and may be of limited usefulness.^{1, 2, 6, 7} Specialized investigations may be less readily available depending on setting, the choice of which should also be made in light of these same factors.^{6, 8}

Step 3 | Determine possible causes and reverse as possible if in keeping with goals of care

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Pulmonary: Airway obstruction, COPD/asthma, damage from chemotherapy, radiation or surgery, emboli, fibrosis, effusion, primary or metastatic tumour.

Cardiac: CHF, CAD, arrhythmias, pericardial effusion.

Neuromuscular: ALS, CVA, poliomyelitis, myasthenia gravis.

Other: Anxiety, fatigue/deconditioning, weakness, pain, severe anemia, infection, carcinomatosis, hepatomegaly, phrenic nerve lesion, peritoneal effusion.

Superior Vena Cava (SVC) obstruction (This is an emergency and requires prompt intervention.)

PRINCIPLES OF MANAGEMENT



When considering a management approach, always balance burden of a possible intervention against the likely benefit (e.g., does the intervention require transfer to another care setting?)

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- Dyspnea may not be due to hypoxia. Use other methods to provide fresh air when O₂ levels are satisfactory
- Utilize anticipatory planning to promote self-care for respiratory distress
- Focus on relaxation and other non-pharmacological techniques
- Opioids are first line of pharmacological treatment

Step 4 | Interventions

LEGEND FOR USE OF BULLETS

Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence, using a modified GRADE process.

| | |
|--|--|
|  | Use with confidence: recommendations are supported by moderate to high levels of empirical evidence. |
|  | Use if benefits outweigh potential harm: recommendations are supported by clinical practice experience, anecdotal, observational or case study evidence providing low level empirical evidence. |
|  | Use with caution: Evidence for recommendations is conflicting or insufficient, requiring further study |
|  | Not recommended: high level empirical evidence of no benefit or potential harm |

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Interventions available in the home and residential care facilities

-  Develop **activity pacing** with techniques to provide energy conservation.^{14,15}
-  **Learn breath control** methods, e.g., pursed lip and diaphragmatic breathing.^{1,6,19}
-  **Small, frequent meals** will reduce abdominal pressure on the diaphragm.¹⁶

Positioning

-  Sit upright, supported by pillow, or forward leaning with arms on table when standing.⁶ When lying on side, position poor lung side down.¹⁶
-  Stabilization of ribcage may help accessory muscles to engage and improve breathing.²⁹
-  Avoid compression of chest and abdomen; position for optimal lung expansion.³⁰
-  Elevate head of bed to a comfortable 15 to 45 degrees, and elevate arms with pillows.^{30,31}

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Support

- ✔ Provide a comprehensive multi-disciplinary care approach when resources are available.^{15, 24, 32, 33}
- ✔ COPD patients, use exercise and pulmonary rehabilitation.²⁴ Tai Chi²⁰ and inspiratory muscle training,²¹ if appropriate and available.
- ⊞ Provide supportive presence when dyspnea distressing; do not leave alone.^{6, 16}
- ⊞ Phone-based coaching may be beneficial to patients and their care-givers.³⁴
- ⊞ Ask YES and NO questions, rather than open-ended, if talking increases dyspnea.¹⁶
- ⊞ Relaxation techniques of guided imagery and therapeutic touch.⁶
- ⊞ Anxiety management and relaxation. Problem solve to avoid panic.^{6, 14, 15}

Environment

- ⊞ Maintain a calm environment.¹⁶
- ⊞ Strive for an air source that is fresh, cool, humidified and free of irritants.¹⁷
- ⊞ Identify and avoid provoking exertion triggers.¹³

Interventions requiring additional equipment or admission to acute care

- ⊞ **Airflow** with room air is sometimes as effective as oxygen¹⁷ such as medical air via mask or nasal prongs.^{22, 23}
- ⊞ **Oxygen** is generally only helpful for hypoxic patients.³⁶
- ✔ Fans to provide airflow,^{1, 6, 15, 16, 24-27} either a hand-held or electric fan for a minimum of five minutes. (This equipment could very likely be obtained in community for minimal cost.)
- ✔ Walking aids.²⁸ Forward leaning on wheeled walkers may help ventilation.^{1, 28}
- ✔ Neuromuscular electric stimulation whenever no practical barriers and if trained provider available.^{1, 15, 28}
- ✔ COPD and motor neuron disease patients, use chest wall vibration only if tolerated and if trained provider available.^{1, 28}

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-  Oral or parenteral opioids are first line pharmacological treatment.³⁵
-  For home oxygen, see program criteria for required oxygen saturation. Consider practical concerns if oxygen is used in the community.

-  For non-hypoxic patients, limit trial of oxygen, e.g., 72 hours.³⁹

Mild level of distress (patient rating of 1 to 3/10 -- mild dyspnea)

-  **Bronchodilators** such as salbutamol, ipratropium for asthma, COPD.^{43, 45}
-  Provide PRN oral or parenteral opioids if dyspnea is only episodic, and provide for breakthrough dyspnea when already on regular opioids.
-  The size of opioid dose should reflect the patient's severity of dyspnea and opioid tolerance. If no prior opioids and mild dyspnea; use **morphine** 2.5 mg immediate release orally every 4 hours PRN or **HYDROmorphine** 0.5 mg immediate release orally every 4 hours PRN.

Moderate level of distress

(patient rating of 4 to 6/10 -- moderate dyspnea)

-  **Bronchodilators** such as salbutamol, ipratropium for asthma, COPD.^{43, 45}
-  For ongoing dyspnea, begin a regular opioid dose with concurrent PRN:
 -  **Morphine** orally: 2.5 mg immediate release every 4 hours.
Morphine parenterally: 1 to 1.5 mg SC or IV every 4 hours.
 -  Alternatively: **HYDROmorphine** 0.5 mg orally every 4 hours, OR **HYDROmorphine** 0.25 mg SC or IV every 4 hours.
 -  Titrate opioid dose incrementally by about 25% according to effectiveness and PRN usage in prior 24 hours. Goal is patient comfort, determined by subjective, objective effect and tolerance.
-  Provide preventative anti-emetic and bowel management to prevent, and to immediately manage, opioid adverse effects of nausea, vomiting and constipation. Incidence may triple with opioid use.³⁷
-  Monitor for excessive opioid-induced drowsiness; use **Pasero Opioid-Induced Sedation Scale (POSS)** assessment tool ([Underlying causes of dyspnea in palliative care](#)).
-  **Corticosteroid** trial in major airway obstruction, lymphangitis carcinomatosa, radiation or drug-induced pneumonitis,¹ or for endotracheal and bronchial tumors.⁴¹ A limited course duration will likely reduce risk of adverse effects. Assess benefit, as current use evidence limited to COPD patients.³⁵
 -  Use short course **corticosteroids** for COPD dyspnea exacerbations.⁴⁰
-  **Benzodiazepines** may assist anxiety or panic,^{1, 35} e.g., with the combination of midazolam and morphine in terminal stage cancer patients with anxiety.^{1, 35}
 -  A systematic review has found no efficacy evidence of benzodiazepines for the relief of breathlessness in patients with advanced cancer or COPD regardless of type of benzodiazepine, dose or route, nor for prevention of breakthrough dyspnea.⁴²
 -  Use benzodiazepines only as a second or third line agent when opioids and non-pharmacological measures have failed to control breathlessness.

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- ☰ **Methotrimeprazine's** role limited to use only as a second line agent or in combination with an opioid when further opioid dose titration is contraindicated.⁴³ Initiate at low doses, monitor for benefit, excessive sedation, and anti-cholinergic side effects such as extrapyramidal effects as reviews have concluded limited to no effectiveness.^{1, 44}

Severe distress

(patient rating of 7 to 10/10 -- severe dyspnea = crisis management)

- ☰ Use opioids and adjunctive anxiolytics/sedatives until comfort is achieved.^{1, 35}
- ☰ Opioid naïve: use morphine 5 mg SC or IV bolus every 5 to 10 minutes. Double dose if no effect every three doses; hold and reassess once dyspnea is reduced, especially if very sedated.¹⁷
- ☰ Opioid tolerant: give full regular opioid dose SC or IV every 5 to 10 minutes. If ineffective, double dose as above.
- ☰ If patient anxious, use one of the following with opioid: either **midazolam 2.5 to 5 mg SC or IV, OR lorazepam 5 mg SC or IV** every 5 to 15 minutes PRN.
- ☰ Use incremental opioid titration first line until patient comfortable. Monitor for effectiveness and excessive sedation using POSS.

Not recommended

- ☒ Administration of nebulized opioids.^{37, 46}

Patient and family education

Refer to non-pharmacological interventions section for more information.

- ☰ Ensure inhalers are being used correctly.
- ☰ Inform patient and family that dyspnea is not always caused by low oxygen levels and may not improve with oxygen. Fresh air via a fan, positioning and opioids may be more helpful than oxygen.
- ☰ Build a documented plan, both for ongoing dyspnea and for acute dyspnea episodes.^{1, 9-13}
- ☰ A symptom and medication diary can be useful.
- ☰ Ask about cultural practices involving smoke and respect decisions to continue these practices.
- ☰ Encourage smoking cessation. Dyspnea can be lessened even after early lung cancer diagnosis.¹⁸
- ☰ Teach safe and appropriate use of medications including purpose, adverse effects and how to manage.¹⁵ Include correct use of inhalers.⁶

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Resources specific to dyspnea

- First Nations Health Authority: “Keep tobacco sacred”
→ <http://www.fnha.ca/wellness/wellness-and-the-first-nations-health-authority/wellness-streams/respecting-tobacco#keep-tobacco-sacred>
- BC Guidelines: Dyspnea (medication table as well)
→ http://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/palliative2_dyspnea.pdf
- BC Cancer Agency: Symptom management guidelines: Dyspnea
→ <http://www.bccancer.bc.ca/nursing-site/Documents/5.%20Dyspnea.pdf>
- BC’s Heart Failure Network: Clinical practice guidelines for heart failure symptom management: Dyspnea
→ <http://www.bcheartfailure.ca/wp-content/uploads/downloads/2015/01/Dyspnea-Jan-20151.pdf>
- Managing dyspnea in patients with advanced chronic obstructive pulmonary disease: a Canadian Thoracic Society clinical practice guideline. ²⁹
→ <http://www.respiratoryguidelines.ca/>

General Resources

- **Provincial Palliative Care Line** – for **physician** advice or support, call **1 877 711-5757** In ongoing partnership with the Doctors of BC, the toll-free Provincial Palliative Care Consultation Phone Line is staffed by Vancouver Home Hospice Palliative Care physicians 24 hours per day, 7 days per week to assist physicians in B.C. with advice about symptom management, psychosocial issues, or difficult end-of-life decision making.
- BC Centre for Palliative Care: Serious Illness Conversation Guide
→ <http://www.bc-cpc.ca/cpc/>
- BC Guidelines: Palliative Care for the Patient with Incurable Cancer or Advanced Disease
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care>
- BC Palliative Care Benefits: Information for prescribers
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program>
- National Centre for Complementary and Alternative Medicine (NCCAM) for additional information on the use of non-pharmacological interventions
→ <https://nccih.nih.gov/>
- Canadian Association of Psychosocial Oncology: Pan-Canadian Practice Guideline: Screening, Assessment and Management of Psychosocial Distress, Depression and Anxiety in Adults with Cancer
→ http://www.capo.ca/wp-content/uploads/2015/11/FINAL_Distress_Guideline1.pdf

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- Fraser Health psychosocial care guideline
→ <https://www.fraserhealth.ca/media/psychosocial%20care.pdf>

Resources specific to health organization/region

- Fraser Health
→ <http://www.fraserhealth.ca/health-professionals/professional-resources/hospice-palliative-care/>
- First Nations Health Authority
→ <http://www.fnha.ca/>
- Interior Health
→ <https://www.interiorhealth.ca/YourCare/PalliativeCare/Pages/default.aspx>
- Island Health
→ http://www.viha.ca/pal_eol/
- Northern Health
→ <https://www.northernhealth.ca/Professionals/PalliativeCareEndofLifeCare.aspx>
- Providence Health
→ <http://hpc.providencehealthcare.org/>
- Vancouver Coastal Health
→ <http://www.vch.ca/your-care/home-community-care/care-options/hospice-palliative-care>

Resources specific to patient population

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians
→ <https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf>
- ALS Society of British Columbia 1-800-708-3228
→ www.alsbc.ca
- BC Cancer Agency: Symptom management guidelines
→ <http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management>
- BC Renal Agency: Conservative care pathway and symptom management
→ <http://www.bcrenalagency.ca/health-professionals/clinical-resources/palliative-care>
- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management
→ <http://www.bcheartfailure.ca/for-bc-healthcare-providers/end-of-life-tools/>

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- Canuck Place Children's Hospice
→ <https://www.canuckplace.org/resources/for-health-professionals/>
 - 24 hr line – 1.877.882.2288
 - Page a Pediatric Palliative care physician – 1-604-875-2161 (request palliative physician on call)
- Together for short lives: Basic symptom control in pediatric palliative care
→ http://www.togetherforshortlives.org.uk/professionals/resources/2434_basic_symptom_control_in_paediatric_palliative_care_free_download

UNDERLYING CAUSES OF DYSPNEA IN PALLIATIVE CARE

All information regarding causes of dyspnea is contained within the body of the document.

MEDICATIONS FOR MANAGEMENT OF DYSPNEA

No medication table included in this document

Prices for prescription drugs may be obtained from BC PharmaCare. The British Columbia Palliative Care Benefits Plan <http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/palliative-formulary.pdf> provides province wide drug coverage for many of the recommended medications— check website to confirm coverage. **Consider price when choosing similarly beneficial medications, especially when the patient / family is covering the cost.**

DYSPNEA MANAGEMENT ALGORITHM

No management algorithm included in this document.

DYSPNEA EXTRA RESOURCES OR ASSESSMENT TOOLS

Pasero Opioid-Induced Sedation Scale (POSS)⁷⁸

| | |
|----------|---|
| S | sleep, easy to arouse |
| 1 | awake and alert |
| 2 | slightly drowsy, easily aroused |
| 3 | frequently drowsy, arousable, drifts off to sleep during conversation |
| 4 | somnolent, minimal or no response to physical stimulation |

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Cough is an important physiological reflex to prevent foreign material entering the lower respiratory tract; it helps to clear excess secretions, microbes and other substances¹⁻⁴ from the lungs and bronchial tree^{2,5} when muco-ciliary transport is insufficient.⁶ Coughing occurs as an explosive expiration that can be a conscious act or a reflex response to an irritation of the tracheobronchial tree.^{7,8} It is also a contributing factor in the spread of infectious disease.²

- **Acute cough** usually lasts less than 3 weeks,⁹⁻¹¹ but can last up to 8 weeks.²
- **Chronic cough** lasts more than 8 weeks and is attributed to distinct malignant and non-malignant diseases.^{2,3,7-10,12} Cough is abnormal when it is ineffective, interferes with quality of life, and causes other symptoms.¹³
- **Dry cough** occurs when no sputum is produced.^{7,8,11}
- **Productive cough** occurs when sputum is produced.^{7,8} Sputum may contain clear secretions, mucous, pus, blood, bronchial casts, or other foreign material.

PREVALENCE

Chronic cough is most common in lung cancer (up to 86%),^{14,15} cancers of the head and neck (over 90%),⁶ and other advanced cancers (up to 40%).^{14,15} It is also very common in advanced chronic diseases,⁶ especially chronic obstructive pulmonary disease (COPD) (up to 70%),¹⁶⁻²¹ and interstitial pulmonary fibrosis (up to 80%).²²⁻²⁴ Cough is significantly more prevalent in smokers²¹ and affects many of those with late stage organ failure (brain, heart, kidney, liver),²⁵ asthma, and HIV infection.^{8,26,27} In lung cancer patients, up to 48% reported moderate to severe cough intensity.²⁸ Considering that up to 86% of patients living with, and dying from, advanced illness experience distressing cough,^{15,29,30} greater attention is required.

IMPACT

Chronic cough can have profound physical and psychosocial impacts on quality of life for both patients and caregivers/family,^{6,9,31} yet it is often undertreated.³² Cough interferes with sleep, oral intake,^{12,33} provokes discomfort,³ and leads to physical exhaustion. It may worsen existing symptoms such as pain, dyspnea, nausea and vomiting,¹² depression,^{34,35} and incontinence.^{12,33,36,37} Cough may also cause new problems, such as rib fractures,^{36,38,39} or lead to life-threatening complications.⁴⁰⁻⁴² Chronic cough is embarrassing for patients, interrupts conversation, stresses relationships and leads to social isolation. Families and friends may find it difficult to tolerate the repetitive noise,^{3,33,37,38} adding to existing burdens. Cachexia and generalized weakness, common near end-of-life, may make coughing more exhausting and less effective.^{6,29,36}

STANDARD OF CARE

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Step 1 | Goals of care conversation

Determine goals of care in conversation with the patient, family and inter-disciplinary team. Refer to additional resources ([Additional resources for management of cough](#)) for tools to guide conversations and required documentation. Goals of care may change over time and need to be reconsidered at times of transition, e.g., disease progression or transfer to another care setting.

Step 2 | Assessment

Ongoing comprehensive assessment is the foundation of effective cough management, including interview (see [Cough management algorithm](#)). Use both objective and subjective measures.^{11, 43} Cough assessment determines the cause, triggers, impact on quality of life, and effectiveness of treatments.^{1, 5, 29, 30, 44-47}

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Cough Assessment: Using Mnemonic O, P, Q, R, S, T, U and V¹

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| Mnemonic Letter | Assessment Questions <i>Whenever possible, ask the patient directly. Involve family as appropriate and desired by the patient.</i> |
|-------------------------------|---|
| O nset | When did it begin? How long does it last? How often does it occur? |
| P rovoking /Palliating | What triggers your cough? What makes it better? What makes it worse? Is it worse in the morning, after a meal, at night? Smoking history/environmental exposures? Is it positional? Can you talk on the phone? Eat? Drink? |
| Q uality | What does it feel like? Can you describe it? Sputum? If yes, what colour/amount/frequency? Does it contain any blood? Does it affect your voice? Cause anxiety? |
| R egion/Radiation | Does it feel like it is coming from your chest or throat? |
| S everity | How severe is this symptom? What would you rate it on a scale of 0-10 (0 being none and 10 being the worst possible)? Right now? At worst? On average? How bothered are you by this symptom? Are there any other symptom(s) that accompany this symptom? (e.g., pain, shortness of breath)? Does your cough affect these? Do you have chills/fever/joint pain? Wheezing? Night sweats/weight loss? Allergies? Reflux? |
| T reatment | What medications and treatments are you currently using? Are you using any non-prescription treatments, herbal remedies, or traditional healing practices? How effective are these? Do you have any side effects from the medications and treatments? What have you tried in the past? Do you have concerns about side effects or cost of treatments? |
| U nderstanding | What do you believe is causing this symptom? How is it affecting you and/or your family? What is most concerning to you? |
| V alues | What overall goals do we need to keep in mind as we manage this symptom? What is your acceptable level for this symptom (0-10)? Are there any beliefs, views or feelings about this symptom that are important to you and your family? |

Symptom Assessment: Physical assessment as appropriate for symptom

Complete history and physical assessment, including oral exam (see [Cough management algorithm](#)). Review medication, medical/surgical conditions, psychosocial and physical environment, including past/present occupation.^{10, 21, 53} Identifying the underlying etiology of the cough is essential in determining the treatment required.^{1, 5, 6, 29, 30, 45, 47, 48, 54-57}

Diagnostics: consider goals of care before ordering diagnostic testing

- Include chest x-ray,^{7, 8, 10, 21, 56, 57} CBC, pulse oximetry,³⁷ and CT scan.^{2, 10}

Step 3 | Determine possible causes and reverse as possible if in keeping with goals of care (For more details, see [Underlying Causes of Cough in Palliative Care](#))

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In almost all cases, cough is a complication of the primary pathology, but unrelated causes should not be automatically excluded.^{3,10} Chronic cough in the palliative population is usually due to multiple pathological mechanisms which are both cancer related and non-cancer.^{6,37,53} (See [Underlying causes of cough in palliative care for more information](#)). Cough may be triggered by a wide variety of chemical (e.g., smoke), inflammatory (e.g., histamine), and mechanical (e.g., sputum or thrush) stimuli,^{51,58} producing a cascade of symptom effects.^{7,49}

PRINCIPLES OF MANAGEMENT



When considering a management approach, always balance burden of a possible intervention against the likely benefit (e.g., does the intervention require transfer to another care setting?)

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- Identify and immediately treat reversible underlying causes ([Underlying causes of cough in palliative care](#) and [cough extra resources or assessment tools](#)) if possible and appropriate.^{6, 12, 50, 56} Often acute cough episodes may be effectively managed.⁵⁵
- Eliminate/reduce triggers to minimize risk of aggravating cough.^{6, 10, 51}
- Start symptomatic treatment for any distressing cough whether waiting for acute treatments to work or when cough is irreversible.^{2, 6, 10}
- Use multiple concurrent therapies to control intractable coughing.³
- Involvement of the multi-disciplinary team is essential to support patient/family coping.^{3, 9}
- The burdens of cough are significant to patients yet shown to be poorly supported.⁴⁹
- Settle productive cough in dying patients.^{6, 29}

Step 4 | Interventions

LEGEND FOR USE OF BULLETS

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Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence, using a modified GRADE process.

| | |
|--|--|
|  | Use with confidence: recommendations are supported by moderate to high levels of empirical evidence. |
|  | Use if benefits outweigh potential harm: recommendations are supported by clinical practice experience, anecdotal, observational or case study evidence providing low level empirical evidence. |
|  | Use with caution: Evidence for recommendations is conflicting or insufficient, requiring further study |
|  | Not recommended: high level empirical evidence of no benefit or potential harm |

Non-pharmacological interventions

Interventions available in the home and residential care facilities

It may be possible to manage cough in the home or residential care facility with appropriate planning and support for the patient, family and staff; all of these interventions do not necessarily require additional equipment or admission to acute care.

For Dry Cough

-  **Speech therapy strategies:**³² pursed lip breathing, replace cough with swallow, relaxed throat breath, cough suppression education,⁵⁹ and distraction.^{67, 68}
-  **Nebulized saline,**^{3, 9, 65, 66} **steam, or cold air humidifier**^{5, 7, 8, 17, 29, 46-48} reduces dryness and irritation of airways. Ensure adequate hydration.³⁰ Avoid fluid overload.

For Productive Cough

-  Use **airway clearance therapies (ACTs)** as appropriate for condition; these include: active cycle of breathing technique (ACBT), autogenic drainage,⁶⁹ and forced expiration to remove secretions. Passive techniques include chest physiotherapy^{3, 21} and postural drainage,^{1, 5, 21, 29, 30, 44, 46, 48, 60} which is not to be used during acute exacerbation of chronic bronchitis.¹
-  **Nebulized saline** reduces viscosity of thick or purulent secretions to aid expectoration.^{37, 62, 63}
-  Suction is usually not indicated except for patients with: tracheostomy, complete esophageal obstruction preventing saliva swallow, bleeding in mouth or throat (use with caution so as not to make it worse), acute fulminant pulmonary edema,^{29, 46} or massively secreting bronchogenic tumour.²¹

Pharmacological interventions Direct drug treatment to identified causes (see [Underlying causes of cough in palliative care](#))

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Mild Cough

Continue non-pharmacological interventions when beneficial

Dry



Demulcents: to soothe irritation, use local anesthetic lozenges or a sweet syrup called 'simple syrup', a mixture of sugar and water, obtained from a pharmacy.^{2, 7, 13, 14, 36, 70-72}



Dextromethorphan^{7, 14, 36, 71, 73} has variable benefit.⁶

Productive



Expectorants: Guaifenesin to liquefy viscous mucous and promote expulsion.^{2, 13, 37}

Moderate to Severe Cough

Continue non-pharmacological interventions

Dry - demulcents when beneficial



Morphine:^{17, 36, 50, 72, 74} start low (e.g., 2.5 to 5 mg IR PO Q4-6H).^{6, 9, 72, 74}



Review of other opioids reveal no demonstrated superiority over morphine.^{59, 72}



Opioids such as HYDROcodone and HYDROmorphine also provide cough suppression.²⁸



Avoid use of codeine: benefit no greater than placebo.⁷⁵⁻⁷⁷ A prior standard of treatment but is now considered either ineffective or provides a highly variable benefit.^{36, 78-80, 81} Morphine preferred as it is unaffected by pharmacogenomic CYP2D6-dependent metabolism.^{6, 74, 82}



Consult palliative specialist if results unsatisfactory. Further options may include nebulized lidocaine when cough is refractory^{41, 72, 78, 83, 84} to add peripheral action to morphine central effects.^{37, 71, 72} Otherwise use methadone or gabapentin.^{14, 21, 70-72, 85}

Productive - may require anticholinergics such as glycopyrrolate or scopolamine at end-of-life.^{4, 10, 14, 86}

(See [Respiratory Congestion](#) guideline for more information.)

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Pharmacological interventions *continued*

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Management

-  Expect maximal morphine benefit within 5 days and, when effective, cough suppression is maintained.⁷⁴
-  Titrate drug doses up to effect/tolerable/maximum doses ([Medications for management of cough](#)).
-  Once established on morphine, to further decrease coughing, trial additional PRN doses,⁹ or an increase of 20-50% of the regularly scheduled morphine dose.^{3, 6}
-  Treat other **existing** symptoms worsened by, **or resulting from**, chronic coughing. Prolonged coughing can cascade into aggravating anxiety, shortness of breath, and fatigue.^{10, 49, 87}
 -  Night time cough management is especially important to provide restful sleep.⁷ Aim to settle cough with drugs before bedtime; give sufficiently early for onset to work.
 -  Dry night cough is common. Just laying down is reported to often trigger coughing.⁴⁹

Patient and family education

-  Provide information regarding the etiology of cough, expectations of treatment, and practical advice to enhance patient and family coping ability.^{29, 59} Discuss fears; acknowledge anxieties.⁹
-  Teach patient and family to develop a self-management plan which may include:
 -  Eliminating environmental irritants⁵⁹ and supporting options for smoking cessation, when applicable.^{1, 30, 46, 54, 60, 61}
 -  Improving ventilation: open window; use a fan⁹; use humidification.⁷
 -  Using positioning, posture, relaxation and anxiety reduction techniques.^{1, 3, 9}
-  Encourage forced expiratory “huffing” to clear secretions^{1, 48, 62, 63} and controlled breathing techniques to reduce cough.^{3, 9, 59}
-  Proper use of medication; value of response monitoring with cough diary.⁷
-  If hemoptysis/risk of massive bleeding, see Severe Bleeding guideline for more information.

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Resources specific to cough

- Airway clearance techniques
→ <https://www.cff.org/Life-With-CF/Treatments-and-Therapies/Airway-Clearance/Airway-Clearance-Techniques/>

General Resources

- **Provincial Palliative Care Line** – for **physician** advice or support, call **1 877 711-5757** In ongoing partnership with the Doctors of BC, the toll-free Provincial Palliative Care Consultation Phone Line is staffed by Vancouver Home Hospice Palliative Care physicians 24 hours per day, 7 days per week to assist physicians in B.C. with advice about symptom management, psychosocial issues, or difficult end-of-life decision making.
- BC Centre for Palliative Care: Serious Illness Conversation Guide
→ <http://www.bc-cpc.ca/cpc/>
- BC Guidelines: Palliative Care for the Patient with Incurable Cancer or Advanced Disease
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care>
- BC Palliative Care Benefits: Information for prescribers
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program>
- National Centre for Complementary and Alternative Medicine (NCCAM) for additional information on the use of non-pharmacological interventions
→ <https://nccih.nih.gov/>
- Canadian Association of Psychosocial Oncology: Pan-Canadian Practice Guideline: Screening, Assessment and Management of Psychosocial Distress, Depression and Anxiety in Adults with Cancer
→ http://www.capo.ca/wp-content/uploads/2015/11/FINAL_Distress_Guideline1.pdf
- Fraser Health psychosocial care guideline
→ <https://www.fraserhealth.ca/media/psychosocial%20care.pdf>

Resources specific to health organization/region

- Fraser Health
→ <http://www.fraserhealth.ca/health-professionals/professional-resources/hospice-palliative-care/>
- First Nations Health Authority
→ <http://www.fnha.ca/>
- Interior Health
→ <https://www.interiorhealth.ca/YourCare/PalliativeCare/Pages/default.aspx>
- Island Health
→ http://www.viha.ca/pal_eol/

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- Northern Health
→ <https://www.northernhealth.ca/Professionals/PalliativeCareEndofLifeCare.aspx>
- Providence Health
→ <http://hpc.providencehealthcare.org/>
- Vancouver Coastal Health
→ <http://www.vch.ca/your-care/home-community-care/care-options/hospice-palliative-care>

Resources specific to patient population

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians
→ <https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf>
- ALS Society of British Columbia 1-800-708-3228
→ www.alsbc.ca
- BC Cancer Agency: Symptom management guidelines
→ <http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management>
- BC Renal Agency: Conservative care pathway and symptom management
→ <http://www.bcrenalagency.ca/health-professionals/clinical-resources/palliative-care>
- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management
→ <http://www.bcheartfailure.ca/for-bc-healthcare-providers/end-of-life-tools/>
- Canuck Place Children's Hospice
→ <https://www.canuckplace.org/resources/for-health-professionals/>
 - 24 hr line – 1.877.882.2288
 - Page a Pediatric Palliative care physician – 1-604-875-2161 (request palliative physician on call)
- Together for short lives: Basic symptom control in pediatric palliative care
→ http://www.togetherforshortlives.org.uk/professionals/resources/2434_basic_symptom_control_in_paediatric_palliative_care_free_download

UNDERLYING CAUSES OF COUGH IN PALLIATIVE CARE^{1, 42, 53, 88-90}

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| 1. Cancer State | |
|--|--|
| <i>Directly caused by primary or secondary cancer</i> | |
| • Airway obstruction by tumour | • Pleural tumor (primary or metastasis) |
| • Lymphangitis carcinomatosa | • Pulmonary parenchymal involvement |
| • Multiple tumour microemboli | • Pulmonary leukostasis |
| • Malignant pleural effusion | • Superior vena cava syndrome |
| <i>Indirectly caused by cancer</i> | |
| • Anorexia-Cachexia syndrome | • Paraneoplastic syndrome |
| • Chemotherapy induced | • Pulmonary aspiration |
| • Chemotherapy induced cardiomyopathy (e.g., Doxorubicin) | • Acute pulmonary embolism** ⁹¹ |
| | • Radiotherapy lung damage |
| 2. Non-Cancer State | |
| <i>Immuno-compromised</i> | <i>Neuromuscular pathology †</i> (applies to all NMP) |
| • Prolonged neutropenia | • Amyotrophic lateral sclerosis (ALS) |
| • HIV with CD4 count less than 200 cells/L | • Cerebral vascular disease (CVA) |
| • End stage weakness | • Hereditary ataxia |
| • heart failure (CHF) | • Late stage dementia (any type) |
| • kidney failure (CRF) | • Muscular Sclerosis (MS) |
| • respiratory failure (COPD or fibrosis) | † If dysphagia, refer to Dysphagia guidelines |
| 3. Unrelated to Primary Disease ⁴¹ | |
| • Asthma | • Gastroesophageal reflux disease (GERD) |
| • Bronchiectasis | • Upper airway cough syndrome |
| • Chronic bronchitis/ bronchospasm | • (non-infectious, rhinosinus post-nasal drip) |
| • Infection – pneumonia, candidiasis (bacterial/fungal) | • Sleep Apnea² |

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| 4. Iatrogenic - Medications | |
|-----------------------------|---|
| Drug Classes | Specific Causative Examples* |
| • ACE Inhibitors | 7 to 15% including Ramipril, Captopril, Perindopril, others |
| • Anticonvulsants | Clobazam 3-7%, Gabapentin 1.8%, Levetiracetam 2-9% |
| • Antidepressants | Duloxetine 3% |
| • Antiretrovirals | Lamivudine 18%, Ritonavir 21.7% |
| • Antihypertensives | Carvedilol 5-8%, Diltiazem 2%, Felodipine 0.8-1.7%, Losartan 17-29% (in hypertensive patients who had already experienced cough while receiving ACE-inhibitor therapy), Telmisartan 1.6-15.6% |
| • Antipsychotics | Aripiprazole 3%, Olanzapine 6%, Quetiapine 3%, Risperidone 2% |
| • Chemotherapy | Abiraterone 10.6-17.3%, Bevacizumab 26-30%, Bleomycin, Busulfan 28% IV, Erlotinib 16-48%, Gefitinib, Letrozole 5-13%, Methotrexate, Sunitinib 27% (renal cell carcinoma), Temozolomide 5%, Trastuzumab 26-43% (metastatic breast cancer) |
| • Inhalational agents | Ipratropium, Salbutamol, Corticosteroids |
| • Opioids | Fentanyl 1%, Oxycodone 1-5% |
| • Other | Amiloride greater than 1% to less than 3%, Celecoxib < 2%, Diclofenac 4%, Ertapenem 1.3%, Everolimus 20-30% (tumors), 7% (Kidney transplant), Filgrastim 14% (myelosuppressive chemotherapy), Influximab 12%, Granisetron 2.2%, Memantine 4%, Midazolam 1.3%, Oxybutynin 1-5%, Pamidronate up to 25.7%, Pancrelipase 6-10%, Pravastatin 1.2-8.2%, Sibutramine 3.8%, Tamsulosin 3.4-4.5%, Testosterone < 3%, Ursodiol 7.1%, Zoledronic acid 12% (hypocalcemia of malignancy), 22% (bone metastasis). |

* There are many medications that are reported to cause cough.⁹² This table provides some examples. Consult pharmacist if additional assistance is required.

** Up to 50% of patients with pulmonary embolism present with a cough.²

Bolded – identifies the causes of cough that are most reversible or treatable.^{9,93}

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| Drug (classification) | Dose, Therapeutic Range | Onset, Adverse Effects, Precautions and Dosing Concerns |
|---|---|---|
| Simple Syrup (for dry cough) | 10 mL PO Q2 to 4 H ⁸⁶ | Safe for use; ³⁶ contents are sugar and water. Monitor use in diabetics. Effectiveness may be limited to time of contact, 20 to 30 minutes. ² Mechanism of action unknown. ⁹ Sugar content may reduce cough reflex by increasing saliva production, swallowing, ⁷ and may act as a protective barrier to sensory receptors in the throat. ^{7, 70} |
| GuaiFENesin (for wet cough) | 200 to 400 mg PO Q4H ^{10, 70, 72, 99} <u>Maximum daily dose:</u> 2400 mg ¹⁰ | Adverse effects: Gastric irritant, may rarely cause nausea and vomiting at higher doses. ^{4, 72} Urolithiasis, headache. ⁴ Contraindicated: Hypersensitivity to guaiFENesin products. Precautions: Not for use for patients who are unable to cough, ^{70, 72} e.g., neuromuscular disease such as amyotrophic lateral sclerosis. ⁶ <u>Do not confuse with guanFACINE (different drug).</u> <u>Not for use in children younger than 6 years.</u> ¹⁰⁰ |
| Dextromethorphan (for dry cough) | 15 to 30 mg PO Q4 to 8H ⁸⁶ <u>Maximum daily dose:</u> 120 mg ^{3, 72, 86} | Onset: 15 to 30 minutes. ¹⁰¹ Adverse effects: Rash, hives, risk of serotonin syndrome. ¹⁰² Uncommon: nausea, drowsiness, vomiting, stomach discomfort, and constipation. ¹⁰¹ Contraindicated: Concurrent or within 14 days of monoamine oxidase inhibitor use. ¹⁰² Precautions with selective serotonin reuptake inhibitors or other medications for depression or Parkinson's disease, or for 2 weeks after stopping the medication. <u>Not for use in children younger than 6 years.</u> ¹⁰⁰ Risk abuse, especially among adolescents, producing euphoria and hallucinations. ¹⁰¹ Metabolized by cytochrome P450 CYP2D6; monitor for potential drug interactions. ^{6, 72} |

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| Drug (classification) | Dose, Therapeutic Range | Onset, Adverse Effects, Precautions and Dosing Concerns |
|---|--|--|
| Morphine † (for dry cough) | <u>Starting dose:</u> 2.5 to 5 mg PO Q4-6H | <p>Adverse effects: Typical opioid side effects such as sedation, constipation, and nausea.¹² Assess for intolerance.</p> <p>Contraindicated: chronic cough due to <u>bronchiectasis</u>.²</p> <p>Precautions: Renal impairment. <u>Do not normally use to manage cough due to known reversible causes</u>.⁷² See Underlying Causes of Cough in Palliative Care and D</p> <p>Dosing: Other routes of administration include IV, SC (reduce oral dose by half).⁷² Sustained release morphine 10 mg Q12H reduced cough by 40%.^{21, 74} When already on morphine, continue and use the existing immediate-release breakthrough analgesic dose (oral if able or subcutaneous equivalent) for the relief of cough. A maximum of 6 doses can be taken in 24 hours for all indications (pain, breathlessness and cough). Titrate both regular and breakthrough doses as required.⁹</p> |
| HYDROcodone (for dry cough) | <u>Starting dose:</u> Controlled release resin complex: 5 mL or one tablet every 8 to 12 hours <u>Maximum daily dose:</u> 10 mL or 2 tablets. ¹⁰³ | <p>Adverse effects: Constipation, drowsiness, nausea.¹⁰³</p> <p>Contraindicated: Chronic cough due to <u>bronchiectasis</u>,² marked hypertension, patients receiving monoamine oxidase inhibitors, pre-existing respiratory depression, intra-cranial lesions with increased intracranial pressure.¹⁰³</p> <p>Precautions: Use with hypnotics/sedatives.¹⁰³ Suspension must not be diluted with fluids or mixed with other drugs because this alters the resin-binding and changes the absorption rate.¹⁰³</p> <p>Dosing: Product is a controlled-release resin complex containing HYDROcodone 5 mg and an antihistamine phenyltoloxamine 10 mg per tablet or 5 mL. The antihistamine may potentiate the antitussive effects of HYDROcodone. HYDROcodone has less antitussive activity than morphine,²⁸ but shown effective at 10mg/day.²¹ HYDROcodone is significantly metabolized into 2 metabolites by cytochrome CYP2D6 (into HYDROmorphone) and CYP3A4 (into active norhydrocodone).¹⁰⁴ Cough suppression effectiveness and toxicity of HYDROcodone may be dependent¹⁰⁴ (unconfirmed) on CYP2D6 metabolism, and a switch to another opioid such as HYDROmorphone or morphine maybe preferred.^{28, 82}</p> |

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|---|---|---|
| HYDROmorphone (for dry cough) | <u>Starting dose:</u> 0.5 to 1 mg PO Q4H Dose Q6H if renal impairment | Adverse effects: Typical opioid side effects such as sedation, constipation, and nausea. ¹² Assess for intolerance. Contraindicated: Chronic cough due to <u>bronchiectasis</u> . ² Precautions: May accumulate in renal impairment, less so than morphine. Dosing: HYDROmorphone is not metabolized by CYP450 enzymes to any great extent ⁸² . |
| Lidocaine 2% † Preservative free (for dry cough) | 2 to 5 mL in 1 mL of normal saline Q4H Nebulized ^{53, 78} <u>Maximum daily dose:</u> 5 mL Q4H | Adverse effects: Well-tolerated, bitter taste, dysphonia, oropharyngeal numbness. ⁷⁸ Precautions: Keep NPO for at least 1 hour after use ^{10, 72} to prevent aspiration risk. May precipitate bronchospasm in asthmatic patients. ^{53, 105} Monitor patients with hepatic disease for toxicity. ⁷⁸ Use with oxygen; a standard pre-dose of salbutamol suggested in 1 case report to mitigate lidocaine-induced bronchospasm. ⁷⁸ Avoid inhalation of preservative containing formulations. Use plain lidocaine sterile parenteral solutions to nebulize. Dosing: Rinse and spit after nebulization to minimize numbness of lips and tongue. ⁵² Use a mouthpiece rather than a mask for inhalation. ⁵² Bupivacaine (0.25% 5 mL nebulized Q4H) has been suggested as an alternative and is also an amide local anesthetic. ^{52,41} |
| Nicotine Patch (smoking cessation aid)  | Apply one patch every 24 hours. Select dose based on smoking use, e.g., 7, 14, 21 mg | Adverse effects: Skin irritation, sleep disturbance. Precautions in heart, thyroid, circulation or stomach problems, stroke or high blood pressure. For patients taking insulin or any prescription medications, consult physician. ¹⁰⁶ Dosing: Assess potential for current drugs levels to increase after stopping cigarette smoking. Hydrocarbons in tobacco smoke induce CYP1A2 metabolism and smoking cessation may increase drug levels of drugs including: olanzapine, fluvoxamine, clozapine, propranolol, caffeine. As other smoking cessation products exist that may be more suitable, review with health care professional. Check patient eligibility for drug product coverage through the BC Smoking Cessation program . |

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| Drug (classification) | Dose, Therapeutic Range | Onset, Adverse Effects, Precautions and Dosing Concerns |
|---|--|---|
| Dexamethasone (Corticosteroid -anti-inflammatory) | Dosing 2 to 16 mg daily, indication specific | <p>For indications: non-asthmatic eosinophilic bronchitis, un-controlled asthma, stridor, tumor-related edema, chronic interstitial lung disease, lymphangitis, radiotherapy/chemotherapy induced pneumonitis carcinomatosis, or superior vena cava obstruction.^{3, 6, 14, 21, 71, 107}</p> <p>Adverse effects: Candidiasis, fluid retention, gastritis, hypokalemia, hyperglycemia, myopathy, insomnia, impaired wound healing, psychosis.^{9, 108, 109} After 6 weeks of use, greater risk of steroid-induced diabetes, proximal myopathy, lipodystrophy (moon face, buffalo hump), and after 3 months, of osteoporosis and glaucoma.¹⁰⁹ For symptomatic gastroprotection while on corticosteroids, if medical history suggests need, use a proton pump inhibitor such as pantoprazole or rabeprazole.</p> <p>Contraindicated when systemic infection, unless considered to be life-saving and specific anti-infective therapy is employed.¹⁰⁹</p> <p>Precautions: Use in patients with psychotic illness (lower dose below 6 mg daily), seizure disorders, hypertension, diabetes.¹⁰⁸</p> <p>Dosing: Assess for potential drug interactions, particularly anticoagulants, anticonvulsants and anticoagulants. Avoid NSAIDs as increases peptic ulceration risk 15-fold together.¹⁰⁹ Reduce dose to the minimum effective dose to avoid side effects.¹¹⁰</p> |

† Off-label. PO = by mouth IV = Intravenous, SC = Subcutaneous, TID = three times daily, QID = four times daily ODT = oral dissolving tablet CSCI = continuous subcutaneous infusion.

Prices for prescription drugs may be obtained from BC PharmaCare. The British Columbia Palliative Care Benefits Plan <http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/palliative-formulary.pdf> provides province wide drug coverage for many of the recommended medications— check website to confirm coverage. **Consider price when choosing similarly beneficial medications, especially when the patient / family is covering the cost.**

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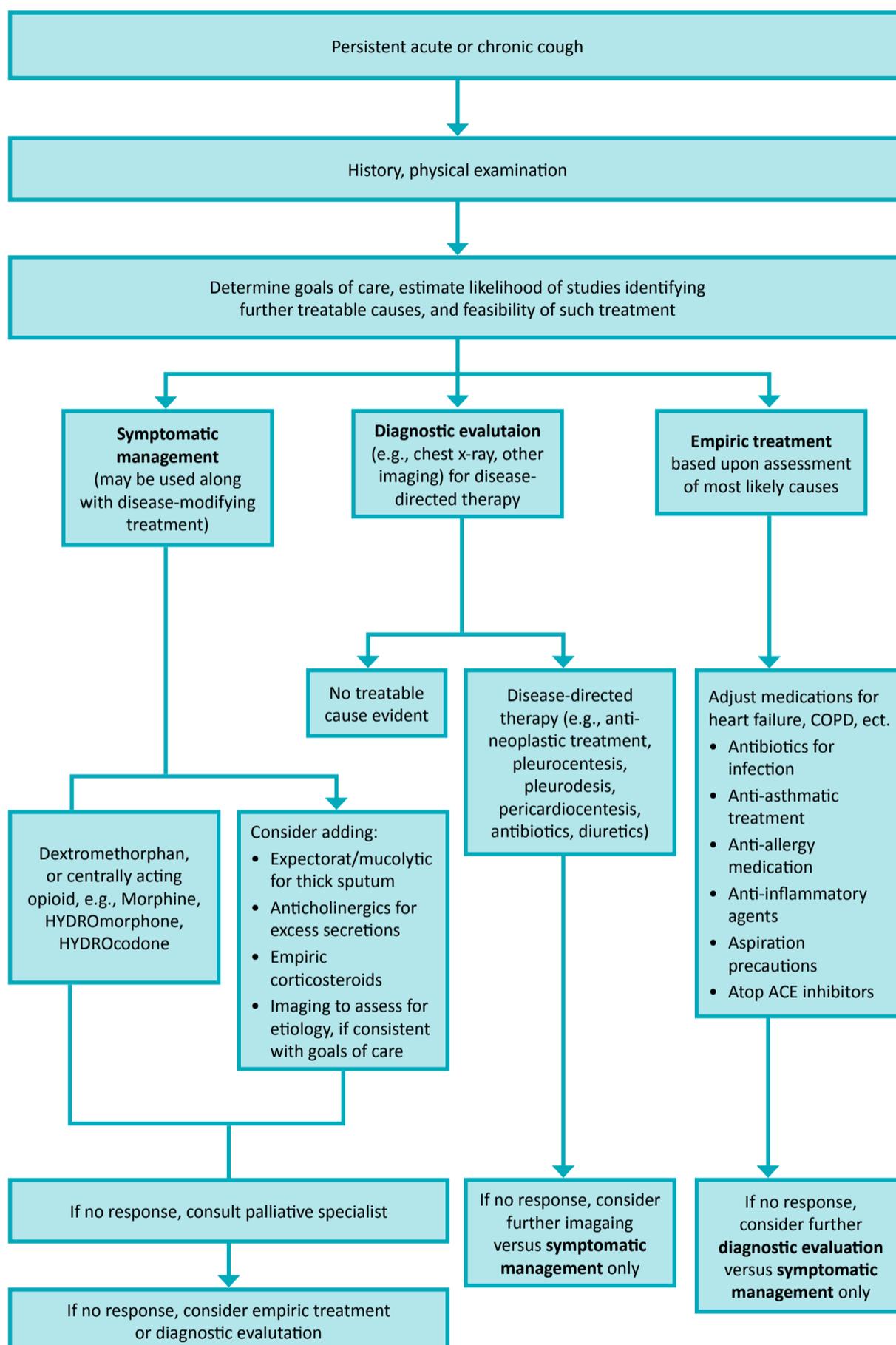
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COUGH EXTRA RESOURCES OR ASSESSMENT TOOLS

Treatments for Common Causes of Cough^{1-3, 5, 6, 9-11, 14, 21, 29, 30, 45, 47, 48, 54, 55, 61, 71, 86, 93-97,98}

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| Underlying Cause | Treatment of Choice |
|--|---|
| ALS | Glycopyrrolate, atropine or scopolamine to dry secretions. (see Additional Resources for Management of Cough) |
| Bronchospasm /Bronchiectasis | Bronchodilators, antibiotics. |
| Chronic Obstructive Pulmonary Disease (COPD) / Asthma | Conventional inhalers/nebulized drugs to dilate airways; cortico-steroids to suppress inflammation. Nebulize saline to reduce viscosity and aid expectoration, if purulent phlegm. |
| Congestive Heart Failure | Conventional medications to decrease excess fluid, e.g., diuretics. |
| End stage weakness | Suppress and settle with suppressant, anxiolytic, glycopyrrolate, atropine or scopolamine. (see Respiratory Congestion guideline) |
| Gastroesophageal reflux | Proton pump inhibitor, H2 inhibitor, motility agent, elevate head of bed, drain contributing ascites. |
| Infection - Pneumonia | Prevention of aspiration. Oral antibiotics may help decrease productive cough that is disturbing sleep, or causing pain or hemoptysis. Nebulized saline may help patients to expectorate thick, tenacious secretions. |
| Malignant pleural effusion | Thoracentesis (with PleurX catheter, if repeated drainage required) or pleurodesis; lying on the same side can decrease related cough. |
| Medications | <ul style="list-style-type: none"> Discontinue; replace ACE inhibitors if possible. May sensitize. Antitussives ineffective to treat. ACE-induced cough. Stop/reduce smoking. Cessation using nicotine patch will minimize airway irritation. |
| Post radiation lung damage | <ul style="list-style-type: none"> Corticosteroids |
| Superior Vena Cava (SVC) obstruction | <ul style="list-style-type: none"> Radiotherapy/corticosteroids |
| Tumor related airway irritation | <ul style="list-style-type: none"> Radiotherapy/brachytherapy, laser treatment, self-expandable stents or corticosteroids. |
| Upper airway cough syndrome (post-nasal drip) – allergies, infection, sinusitis | <ul style="list-style-type: none"> Nasal corticosteroids or ipratropium. Oral antibiotics for sinusitis, expectorants (guaifenesin) or anti-histamine. |

Bolded – identifies the causes of cough that are most reversible or treatable.^{9, 93}

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DEFINITION

Hiccoughs are repeated, involuntary spasmodic contractions of the diaphragm and inspiratory muscles followed by sudden closure of the glottis.¹⁻⁷ Hiccoughs are categorized according to duration^{2,3,4,5,8,9}:

Acute – Hiccoughs that last < 48 hours and are common, non-pathologic, and self-limited.¹⁰

Persistent - Hiccoughs lasting 2 days or more.

Intractable – Hiccoughs that last more than 1 month and not responsive to treatments.

PREVALENCE

Persistent or intractable hiccoughs often indicate serious underlying pathology and are most common (10-20%)⁴ in those with gastro-intestinal tract, thoracic, or central nervous system disease.^{3,5,9-11} Prevalence is relatively low (~1-9%) in the general palliative population.^{2,9,12-18}

IMPACT

Persistent and intractable hiccoughs can interfere with normal daily activity,^{5,19} significantly reducing quality of life, causing distress for both patient and family.⁴ Potential impacts include: increased anxiety, distress,⁷ insomnia, fatigue,^{5,20} gastrointestinal reflux, weight loss, vomiting, aspiration pneumonia, dehydration, electrolyte imbalance, cardiac arrhythmias,²¹⁻²⁵ isolation, delirium (in the elderly), wound dehiscence (in post-surgery),^{3,9} depression, and in rare situations, death.^{23,26-30}

STANDARD OF CARE

Step 1 | Goals of care conversation

Determine goals of care in conversation with the patient, family and interdisciplinary team. Refer to additional resources ([Additional resources for management of hiccoughs](#)) for tools to guide conversations and required documentation. Goals of care may change over time and need to be reconsidered at times of transition, e.g., disease progression or transfer to another care setting.

Step 2 | Assessment

Hiccough Assessment: Using Mnemonic O, P, Q, R, S, T, U and V⁷¹

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| Mnemonic Letter | Assessment Questions <i>Whenever possible, ask the patient directly. Involve family as appropriate and desired by the patient.</i> |
|-------------------------------|--|
| O nset | When did the hiccoughs begin? How long do they last? How often do they occur? |
| P rovoking /Palliating | What brings them on? What makes them better? What makes them worse? |
| Q uality | What do they feel like? Can you describe them? Do they change when you change position? |
| R egion/Radiation | Not applicable |
| S everity | How severe is this symptom? What would you rate it on a scale of 0-10 (0 being none and 10 being the worst possible)? Right now? At worst? On average? How bothered are you by this symptom? Are there any other symptom(s) that accompany this symptom (e.g., nausea, anxiety or fatigue)? |
| T reatment | What medications and treatments are you currently using? Are you using any non-prescription treatments, herbal remedies, or traditional healing practices? How effective are these? Do you have any side effects from the medications and treatments? What have you tried in the past? Do you have concerns about side effects or cost of treatments? |
| U nderstanding | Do they interfere with your ability to eat, drink, talk or enjoy other activities? Do they interfere with your sleep? What do you believe is causing this symptom? How are the hiccoughs affecting you and/or your family? What is most concerning to you? |
| V alues | What overall goals do we need to keep in mind as we manage this symptom? What is your acceptable level for this symptom (0-10)? Are there any beliefs, views or feelings about this symptom that are important to you and your family? |

Symptom Assessment: Physical assessment as appropriate for symptom

Diagnostics: consider goals of care before ordering diagnostic testing

Recognize that hiccoughs can be multifactorial in advanced disease and that an extensive workup to find the cause can be harmful. Consider patient status and goals of care in determining extent of diagnostics required.⁸

- Perform a detailed history and physical.^{4,9}
- Review prior surgical interventions; respiratory and gastrointestinal symptoms; infections; and use of alcohol and medications, especially corticosteroids, benzodiazepines, and barbiturates.¹⁸
- Consider CBC, electrolytes, and chest xray.⁹ Include liver ultrasound and liver function tests, serum Calcium,^{10, 26, 31} CT, MRI and electrocardiography, as needed.⁴
- Invasive tests such as lumbar puncture and bronchoscopy, depend on the patient's situation.²⁶

Step 3 | Determine possible causes and reverse as possible if in keeping with goals of care (For more details, see [Underlying causes of hiccoughs in palliative care](#))

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Over 100 underlying diseases have been associated with hiccoughs.^{1,31} Persistent hiccoughs should be taken seriously as they often indicate underlying pathology.

Common causes of persistent and intractable hiccoughs include^{1,2,4,32,33}

- Gastric stasis and distention (most common)³⁴
- Gastro-esophageal reflux³⁴
- Metabolic disturbances (e.g., uremia, hypercalcemia, low magnesium)¹⁵
- Infection
- Irritation of the diaphragm or phrenic nerve
- Hepatobiliary disease/hepatomegaly
- Cerebral causes (e.g., tumour, metastasis, CVD)⁸

Other important causes

- Myocardial Infarction, pericarditis, aneurysm.^{2,7,8,35}
- Medications such as benzodiazepines, opioids, corticosteroids.² Risk with dexamethasone is 25%.^{15,19} (See [Underlying causes of hiccoughs in palliative care](#) for a list of medication causes)
- Chemotherapy, radiotherapy, and surgery^{15,18,26,37-39}; nasal, pharyngeal, laryngeal conditions; foreign body in ear canal.²
- Anxiety, stress or over-excitement; psychogenic.^{2,7}

PRINCIPLES OF MANAGEMENT



When considering a management approach, always balance burden of a possible intervention against the likely benefit (e.g., does the intervention require transfer to another care setting?).

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- Hiccoughs may resolve on their own; try simple physical techniques.
- Try non-pharmacological interventions during acute 48 hours “bout” phase, particularly any that the patient has previously found helpful.
- Consider medications when they are persistent, lasting more than 48 hours.
- Consider the patient’s general condition to avoid potential side effects.⁸
- Refer to palliative care consultants when refractory or patient unable to swallow.

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LEGEND FOR USE OF BULLETS

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Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence, using a modified GRADE process.

| | |
|--|--|
|  | Use with confidence: recommendations are supported by moderate to high levels of empirical evidence. |
|  | Use if benefits outweigh potential harm: recommendations are supported by clinical practice experience, anecdotal, observational or case study evidence providing low level empirical evidence. |
|  | Use with caution: Evidence for recommendations is conflicting or insufficient, requiring further study |
|  | Not recommended: high level empirical evidence of no benefit or potential harm |

Non-pharmacological interventions

A wide range of non-pharmacological approaches have been used to treat persistent and intractable hiccoughs; however, their safety and efficacy are unknown as no systematic reviews or clinical trials were found.^{8,13} Most treatments have a physiological basis that interrupts the hiccough reflex arc by stimulation of the vagus or phrenic nerves to interfere with normal respiration, or increase pCO₂ levels.⁴

Interventions available in the home and residential care facilities

-  **Breathe holding** or **drinking** in small sips.^{8,13, 33}
-  **Sip** iced water or **swallow** crushed ice.³³
-  **Breathe into a paper bag**, particularly if patient is hyperventilating.³³
-  **Behavioral techniques** such as distraction, small meals, fasting and vigorous exercise (may not be an option in frail elderly or advanced disease patients).⁹
-  **Rub** the soft palate (e.g., with a swab) to stimulate the nasopharynx.³³ Caution as this may trigger gag reflex.

Interventions requiring additional equipment or admission to acute care

-  **Nebulized normal saline** — 2ml of NaCl 0.9% nebulized over 5 minutes at regular intervals throughout the day and prn at night. 43 Needs more study but safe; permits patient self-care and could be considered before drug treatment where equipment is available. **Note: in community, may be able to rent or borrow a home nebulizer machine.**
-  **Acupuncture**,^{1,9,33} if available and acceptable to the patient.
-  **Surgical treatment** has shown benefit when cause is known and possibly removable. Cervical phrenic nerve block, only as last resort.³⁸ Careful patient selection required. Consider implications for overall quality of life. Rarely indicated in the frail elderly⁹ or advanced disease patient.

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A systematic review found little high-level evidence for either non-pharmacological or pharmacological interventions that are effective or harmful.²⁵ Palliative experts lack consensus of medications considered essential for safe and effective hiccup management and acknowledge that additional research is needed.⁴⁴

As hiccoughs often terminate spontaneously,^{25,32,45} drug therapy usually is not indicated unless persistent.

Direct treatment to underlying cause of the condition whenever possible.^{6,9,50,60} Baclofen and gabapentin have a lower risk of long term side effects than neuroleptic agents.⁵⁰ They are now preferred over chlorpromazine which can be poorly tolerated.^{8,41,51}

Baclofen

-  Supported by two small RCTs,^{40,46} and several case reports.^{38,40,46-48} It is suggested to have the best ability to treat hiccoughs.^{1,9} Has been used in cancer and palliative patients with success.^{38,45,47,49}
-  Single doses of baclofen 10 mg have successfully stopped hiccoughs after 0.5 to 3 hours.⁴⁷ This may provide immediate patient comfort if a diagnostic process takes several days.⁴⁷
-  Ongoing dosing of baclofen 10 mg bid, up to 10 mg TID, may be indicated for 2 to 5 days.⁴⁷
-  Use for a longer duration is indicated if unable to remove triggering cause.⁴⁷

Gabapentin

-  May be preferred in hiccoughs related to CNS disease or if neuropathic pain coincides.^{50,51} Has been shown to be effective with advanced cancer patients.¹⁵

Adjunctive therapy

-  Antiemetics may be required if vomiting accompanies hiccoughs.⁴
-  Anxiolytics (e.g., midazolam) if hiccough distress is severe.^{25,24} Consider in last days of life.

For more information, see [Medications for Management of Hiccoughs](#).

Patient and family education^{1,8,20,32,33,41,42}

-  Hiccoughs that last < 48 hours usually resolve on their own.
-  Hiccoughs are often caused by gastric distention, carbonated beverages, alcohol, hot or cold drinks, anxiety or stress.
-  Simple non-drug approaches may be helpful, especially if helped in the past.
-  Draw from strategies identified in non-pharmacological interventions.
-  Contact healthcare provider for hiccoughs that interfere with sleep, or > 2 days.

ADDITIONAL RESOURCES FOR MANAGEMENT OF HICCOUGHS

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Resources specific to Hiccoughs

No additional resources specific to hiccoughs included in this document

General Resources

- **Provincial Palliative Care Line** – for **physician** advice or support, call **1 877 711-5757** In ongoing partnership with the Doctors of BC, the toll-free Provincial Palliative Care Consultation Phone Line is staffed by Vancouver Home Hospice Palliative Care physicians 24 hours per day, 7 days per week to assist physicians in B.C. with advice about symptom management, psychosocial issues, or difficult end-of-life decision making.
- BC Centre for Palliative Care: Serious Illness Conversation Guide
→ <http://www.bc-cpc.ca/cpc/>
- BC Guidelines: Palliative Care for the Patient with Incurable Cancer or Advanced Disease
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care>
- BC Palliative Care Benefits: Information for prescribers
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program>
- National Centre for Complementary and Alternative Medicine (NCCAM) for additional information on the use of non-pharmacological interventions
→ <https://nccih.nih.gov/>
- Canadian Association of Psychosocial Oncology: Pan-Canadian Practice Guideline: Screening, Assessment and Management of Psychosocial Distress, Depression and Anxiety in Adults with Cancer
→ http://www.capo.ca/wp-content/uploads/2015/11/FINAL_Distress_Guideline1.pdf
- Fraser Health psychosocial care guideline
→ <https://www.fraserhealth.ca/media/psychosocial%20care.pdf>

Resources specific to health organization/region

- Fraser Health
→ <http://www.fraserhealth.ca/health-professionals/professional-resources/hospice-palliative-care/>
- First Nations Health Authority
→ <http://www.fnha.ca/>
- Interior Health
→ <https://www.interiorhealth.ca/YourCare/PalliativeCare/Pages/default.aspx>
- Island Health
→ http://www.viha.ca/pal_eol/

Additional resources for management of hiccoughs continued on [next page](#)

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- Northern Health
→ <https://www.northernhealth.ca/Professionals/PalliativeCareEndofLifeCare.aspx>
- Providence Health
→ <http://hpc.providencehealthcare.org/>
- Vancouver Coastal Health
→ <http://www.vch.ca/your-care/home-community-care/care-options/hospice-palliative-care>

Resources specific to patient population

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians
→ <https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf>
- ALS Society of British Columbia 1-800-708-3228
→ www.alsbc.ca
- BC Cancer Agency: Symptom management guidelines
→ <http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management>
- BC Renal Agency: Conservative care pathway and symptom management
→ <http://www.bcrenalagency.ca/health-professionals/clinical-resources/palliative-care>
- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management
→ <http://www.bcheartfailure.ca/for-bc-healthcare-providers/end-of-life-tools/>
- Canuck Place Children's Hospice
→ <https://www.canuckplace.org/resources/for-health-professionals/>
 - 24 hr line – 1.877.882.2288
 - Page a Pediatric Palliative care physician – 1-604-875-2161 (request palliative physician on call)
- Together for short lives: Basic symptom control in pediatric palliative care
→ http://www.togetherforshortlives.org.uk/professionals/resources/2434_basic_symptom_control_in_paediatric_palliative_care_free_download

UNDERLYING CAUSES OF HICCOUGHS IN PALLIATIVE CARE ^{2,5,7,8,38,45}

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| | | | |
|------------------------|-----------------------------|-----------------------|------------------|
| Alcohol | Cyclophosphamide | Gemcitabine | Muscle relaxants |
| Anabolic steroids | Chorionic Gonadotropin | Heroin | Nicotine |
| Aprepitant | Corticosteroids | Hydrocodone | Paclitaxel |
| Aripiprazole | Dexamethasone** | Irinotecan | Perphenazine |
| Barbiturates | Donepezil | Levodopa | Pergolide |
| Benzodiazepines | Docetaxel | Macrolide antibiotics | Progesterone |
| Bupivacaine epidural | Doxycycline | Megestrol | Rocuronium |
| Carboplatin | Ethosuximide | Methotrexate | Sulfonamides |
| Cefotetan | Etomidate | Methylprednisolone | Triamcinolone |
| Chlordiazepoxide | Etoposide | Mexiletine | Vinorelbine |
| Chemotherapy* | Fluoroquinolone antibiotics | Midazolam | Zolpidem |
| Cisplatin | Flumazenil | Morphine | |

* Chemotherapy may be falsely attributed as a cause because dexamethasone is often used concurrently.⁵²

** May be dose-related; more prevalent at dexamethasone doses greater than 10 mg daily.⁵²

MEDICATIONS FOR MANAGEMENT OF HICCOUGHS

There are no approved medications for hiccough use in Canada; everything is off-label.

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| Drug, Action | Dose, therapeutic range | Onset, Adverse Effects, Precautions and Dosing Concerns |
|---|---|--|
| Baclofen 1 st line empiric ^{8,31,38,40,41,50,53,54} | 5 to 20 mg PO every 6 to 12 hour, up to 40 mg/day | Drowsiness, dizziness, hypotension, confusion, nausea, ataxia. Alcohol and CNS depressants can be additionally sedating. Avoid in renal failure, or carefully adjust dose due to risk of delirium, respiratory depression. Risk of withdrawal symptoms when abruptly stopped. Use caution in patients with epilepsy. |
| Gabapentin 1 st line empiric ^{8,15,51,50} | 100 mg TID to QID to start then titrated up until results are seen, maximum 1200 mg/day | Drowsiness, dizziness, fatigue, ataxia, peripheral edema, visual disturbances, clumsiness/unsteadiness. Adjust dose for reduced renal function. No hiccough treatment studies in renal impairment. In extended therapy, when possible, gradually reduce dose over a minimum of one week. Very few drug interactions |
| Metoclopramide 2 nd line empiric ^{32,41,50,55,56} | 10 mg PO,IV,SC TID to QID | Asthenia, headache, drowsiness, fatigue. Serious: tardive dyskinesia, neuroleptic malignant syndrome. Adjust dose for reduced renal function. Avoid concurrent use with: <ul style="list-style-type: none"> Peppermint water (opposing actions on gastro-esophageal sphincter). Haloperidol due to increased risk of extrapyramidal symptoms. GI hemorrhage, mechanical obstruction, or perforation or if GI stimulation might be dangerous. Parkinson disease. Use caution in patients with epilepsy. Oral metoclopramide is 50-80% bioavailable, consider reducing SC, IV, IM dose by 25-50%. |
| Domperidone 2 nd line empiric ^{2,32,50,55} | 10 mg TID to QID | Adverse effects; xerostomia, serious is prolonged QT interval, sudden cardiac death, ventricular arrhythmia. Risk of QT interval prolongation at doses greater than 30 mg/day. Check concurrent drugs for QTc risk. |
| Pantoprazole ^{41,57} | 40 mg daily to BID | Generally safe. Few drug interactions compared to other PPIs. Concomitant use of antacids does not affect the pharmacokinetics of pantoprazole sodium. |
| Antacid containing simethicone ³² | 10 mL QID | |
| Gaviscon ⁵⁰ | 10 mL TID | Give after meals. |

Medications for management of hiccoughs continued on [next page](#)

OTHER PROPOSED DRUG TREATMENTS

(Recommended Only After Palliative Care Consultation)

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| Medication | Dose | Adverse Effects, Precautions and Dosing Concerns |
|--|---|---|
| Amantadine ^{58,59} | 100 mg PO once or twice daily | Non-sedating. Adjust dose for renal function. Three cases (one was cancer/end of life). |
| Chlorpromazine ^{5,8,9,41,50-52,60,61} | 25 to 50 mg PO once daily, titrating up to 3 or 4 times daily | Hypotension, sedation, urinary retention, glaucoma, delirium, extrapyramidal symptoms. Assess risk of QTc prolongation, often concerning. Poorly tolerated in elderly patients. Avoid long term due to risk of tardive dyskinesia. Injection discontinued, no longer available in Canada. Only 25, 50 and 100 mg tablets available. |
| Dexamethasone ^{5,33,62} | 4 up to 8 mg PO daily | Fatigue, sleep disturbance, hiccoughs. Suggested for hepatic or cerebral tumor – to reduce compression/irritation. Few studies. |
| Haloperidol ^{9,56,63} | 0.5 to 5 mg PO TID Or via SC, IV, IM routes | Avoid concurrently with metoclopramide due to increased risk of extrapyramidal symptoms. Recommended dosing from references varies widely. Older studies used IM route, effectiveness via other routes uncertain, but much less painful. Oral haloperidol is 60-70 % bioavailable, consider reducing SC, IV, IM dose by one-third. |
| Lidocaine 2% viscous ^{55,64} | 5 mL orally BID to TID | Single case report. Was swallowed in 3 patients; 2 used with baclofen. May impair swallowing, enhancing aspiration risk. Avoid food ingestion for 60 minutes. |
| Lidocaine ^{1,5,41} | 1 mg/kg loading dose followed by infusion of 2 mg/min CSCI | Risk of cardiovascular and neurologic toxicities. |
| Methotrimeprazine ³² | 3 to 6 mg PO,SC,IV HS | Injectable alternative to chlorpromazine or haloperidol |
| Midazolam ^{5,24,33,56} | 5 to 10 mg SC or PO Q4H PRN CSCI: 10 up to 120 mg/day | Two case reports. Review use and suitability with local palliative care team. Adverse effects include sedation, risk of apnea paradoxical reactions, drug interactions, especially with opioids. reduced elimination in liver or heart failure, and elderly |
| Olanzapine ^{60,65,66} | 2.5 to 7.5 mg PO daily | Three cases reports. In two, used in combination with baclofen as 5 mg baclofen BID, other 10 mg TID. |
| Pregabalin ^{50,67,68,69} | 25 to 75 mg PO BID, up to 375 mg/day | Drowsiness (might be less than gabapentin), dizziness, peripheral edema. Three case reports. |

Other proposed drug treatments continued on [next page](#)

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(Recommended Only After Palliative Care Consultation)

| Medication | Dose | Adverse Effects, Precautions and Dosing Concerns |
|-------------------------------|---|---|
| Sertraline ⁷⁰ | 50 to 150 mg PO/day | Single patient case report. |
| Valproic acid ^{5,50} | 15 to 20 mg PO per kg/24 hours, divided in 1 or 3 doses | May increase by 250 mg/week until hiccoughs stop. |

† Off-label. PO = by mouth IV = Intravenous, SC = Subcutaneous, TID = three times daily, QID = four times daily ODT = oral dissolving tablet, CSCI = continuous subcutaneous infusion.

Prices for prescription drugs may be obtained from BC PharmaCare. The British Columbia Palliative Care Benefits Plan (<http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/palliative-formulary.pdf>) provides province-wide drug coverage for many of the recommended medications; check website to confirm coverage. Consider price when choosing similarly beneficial medications, especially when the patient/family is covering the cost.

HICCOUGH MANAGEMENT ALGORITHM

No management algorithm included in this document.

HICCOUGH EXTRA RESOURCES OR ASSESSMENT TOOLS

No extra resources or assessment tools included in this document.

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TWITCHING/ MYOCLONUS/ SEIZURES

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DEFINITIONS³

Twitching refers to an involuntary muscle contraction; it tends to be repetitive, unwanted, and lacking obvious cause.

Myoclonus is defined as involuntary single or irregularly repetitive movement of one part of the body associated with either brief, shock-like muscle contractions or jerks (positive myoclonus), or brief loss of muscle tone (negative myoclonus). Hiccough is a type of myoclonus. Myoclonus may precede onset of opioid-induced neurotoxicity.³³

Opioid-induced neurotoxicity is due to the accumulation of toxic metabolites. Impaired renal function, dehydration and electrolyte imbalances contribute to this condition. It may cause myoclonus and seizures.³³

Seizures may be varying in intensity and type and may include an absent stare, muscle rigidity, cyanosis, and an altered state of consciousness. They may last from 1-4 minutes.

Status epilepticus is a seizure lasting 5 minutes or longer, or repeated seizures one after another without regaining consciousness.

PREVALENCE

Myoclonus occurs more commonly (2.8-87%) in patients on higher doses of opioids,¹ or in the presence of renal failure²; however, causes can be multifactorial. **Seizures** may be the first indication of a brain tumour. They occur in up to 50% of palliative patients with a primary brain tumour,³ and in 20-45% of patients with brain metastases.^{4, 5}

IMPACT

Twitching and myoclonus may be misinterpreted as seizure activity. Seizures can be frightening for the patient and family. Indicators of neurotoxicity may require switching of opioids.³³

STANDARD OF CARE

Step 1 | Goals of care conversation

Determine goals of care in conversation with the patient, family and interdisciplinary team. Refer to additional resources ([Additional resources for management of seizures](#)) for tools to guide conversations and required documentation. Goals of care may change over time and need to be reconsidered at times of transition, e.g., disease progression or transfer to another care setting.

Step 2 | Assessment

Twitching, myoclonus and seizures assessment: Using Mnemonic O, P, Q, R, S, T, U and V³²

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| Mnemonic Letter | Assessment Questions <i>Whenever possible, ask the patient directly. Involve family as appropriate and desired by the patient.</i> |
|-------------------------------|---|
| O nset | When did it begin? How long does it last? How often does it occur? |
| P rovoking /Palliating | What brings it on? What makes it better? What makes it worse? Have you recently started any new medications or treatments? |
| Q uality | What does it feel like? Can you describe it? How do you feel afterwards? |
| R egion/Radiation | Does your entire body move? Is the movement only in a part of your body? Ask family or caregivers to describe what happens. |
| S everity | How severe is this symptom? What would you rate it on a scale of 0-10 (0 being none and 10 being the worst possible)? Right now? At worst? On average? How bothered are you by this symptom? Are there any other symptom(s) that accompany this symptom? |
| T reatment | What medications and treatments are you currently using? Are you using any non-prescription treatments, herbal remedies, or traditional healing practices? How effective are these? Do you have any side effects from the medications and treatments? What have you tried in the past? Do you have concerns about side effects or cost of treatments? Have you recently changed a dose or type of treatment? Have you stopped or started alcohol or other substances? |
| U nderstanding | What do you believe is causing this symptom? How is it affecting you and/or your family? What is most concerning to you? |
| V alues | What overall goals do we need to keep in mind as we manage this symptom? What is your acceptable level for this symptom (0-10)? Are there any beliefs, views or feelings about this symptom that are important to you and your family? |

Symptom Assessment: Physical assessment as appropriate for symptom

Diagnostics: consider goals of care before ordering diagnostic testing

Degree of investigation depends on severity and goals of care, including desired location.¹⁶ May reveal more than one cause.

- CBC and biochemical tests may reveal reversible causes.
- CSF culture for infectious causes.
- Radiologic: CAT scan or MRI.
- Electroencephalogram if suspect seizure activity, but may not be needed.⁸

Step 3 | Determine possible causes and reverse as possible if in keeping with goals of care

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- Identifying the underlying etiology of the myoclonus, twitching or seizures is essential in order to provide the appropriate treatment.^{3,6}
- Opioid-induced myoclonus is often misinterpreted as seizure activity by caregivers and clinicians.¹ This is important as myoclonus tends to respond to correction of the underlying reversible causes.⁷
- Terminal delirium can also be misinterpreted as seizure.¹
- Impaired excretion of opioids and their metabolites may cause myoclonus.
- Most prevalent in renal impairment with morphine, codeine, meperidine and, to a lesser extent, hydromorphone.¹ Liver impairment also a risk factor.⁹ Methadone or fentanyl rarely cause myoclonic neurotoxicity.^{1,7,10,11}
- Drug causes are extensive and include: tricyclic antidepressants, serotonin reuptake inhibitors, anticonvulsants, ertapenem, pregabalin, trazodone, and levodopa.^{12,13}
- Assess for drug interactions that may contribute to neurotoxicity, e.g., from antipsychotics, antidepressants, and other central nervous system drugs.^{13,14}
- Fully review drugs recently introduced, discontinued, or dosing altered. Especially assess benzodiazepines, alcohol, opioids, anticonvulsants, smoking, caffeine, and complementary or alternative medicines.
- Dehydration may be a contributing factor.⁷
- Other causes may include: pinched nerve, nerve injury, stimulant abuse, epilepsy, Parkinson's disease, amyotrophic lateral sclerosis, and benign fasciculation syndrome.³

Seizure

- Seizures may be caused by primary or metastatic brain tumours.³
- Metabolic causes: hypoglycemia (most common metabolic cause), hyperglycemia, hyponatremia, renal or hepatic failure, and hypercalcemia.
- Hypoglycemia can also be caused by prolonged seizure activity.³
- A wide variety of other causes may be identified including stroke, sepsis or late onset epilepsy.

PRINCIPLES OF MANAGEMENT



When considering a management approach, always balance burden of a possible intervention against the likely benefit (e.g., does the intervention require transfer to another care setting?)

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- Lorazepam is the first-line for all 3 conditions.
- Ensure patient safety and comfort during and following a seizure.
- Twitching/myoclonus is frequently related to opioids and is often reversible.
- Educate patient and family to discern between myoclonus and seizure activity, and to report to their health care team.

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LEGEND FOR USE OF BULLETS

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Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence, using a modified GRADE process.

| | |
|--|--|
|  | Use with confidence: recommendations are supported by moderate to high levels of empirical evidence. |
|  | Use if benefits outweigh potential harm: recommendations are supported by clinical practice experience, anecdotal, observational or case study evidence providing low level empirical evidence. |
|  | Use with caution: Evidence for recommendations is conflicting or insufficient, requiring further study |
|  | Not recommended: high level empirical evidence of no benefit or potential harm |

Non-pharmacological interventions

Interventions available in the home and residential care facilities

-  Recognize that myoclonus or seizures can increase pain, fatigue, and other distressing symptoms. **Follow-up assessment and appropriate intervention.**¹⁵
-  Myoclonus generally responds to **conservative treatment:** correct dehydration and renal function, if possible; and reduction and/or rotation of opioid.^{7,12}
-  **Seizure treatment will vary** according to the frequency and duration of convulsions, and whether there is a reversible underlying cause.⁸
-  **Position HOB 30°** above level of heart if increased cerebral pressure.⁵

Prevention/risk reduction

-  Screen for recent history of recreational drug and alcohol use.
-  Review medication for those that reduce seizure threshold, or reduce effectiveness of current meds. Adjust medications and doses appropriately.^{22,23} Monitor drug levels as required for patient status and location of care.
-  Prevent, monitor for, and minimize adverse effects.

Physiotherapy and occupational therapy

-  Mobility and transfer safety. Referral for assessment, patient/family education and recommendations.¹⁵

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Interventions that may require additional equipment or transfer to acute care

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Environment – injury prevention and maintenance of airway during a seizure.

-  As per local seizure protocol.
-  Ensure potential aggressive treatments align with patient goals of care and consider patient status and location: hydration; intubation and transfer to ICU.⁸
-  Some treatments may be more appropriate earlier in disease trajectory, for short durations to achieve symptom control, or to meet a specific goal.

Hydration

-  Consider for reversible causes of myoclonus². Depends on patient status, goals of care, and care location. Limited evidence of benefit. Requires further study.¹⁷

Surgical

-  Resection of lesion with clear margins has been successful in patients with primary, low grade brain tumours. Remission of seizures in 80% of patients.¹⁸
-  Careful consideration must be given to the life expectancy and appropriateness for patient.¹⁵
-  May allow eventual weaning from long-term anti-consultants after excision.⁸

Radiation Therapy

-  Seizure control can be improved in primary tumors when radiation therapy is offered early, even if no survival benefit.^{19,20,21}

Oxygen

-  Status epilepticus patients benefit from oxygen,¹⁶ if available and if patient is NOT actively dying. Hypoxia is a risk with longer seizures and can result in significant impairment.

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 **Lorazepam** is a first-line therapy for twitching, myoclonus and seizures. Advantages include: rapid onset, sustained duration of action, 85-89% response rate in tonic-clonic seizures, lower cardiorespiratory depression than diazepam, familiarity and availability throughout patient care settings.^{1,2}

 Use non-oral routes of administration often to ensure reliable effectiveness.

Initial Management with Lorazepam³

| Myoclonus/ Twitching | Partial Seizure | Tonic-Clonic Seizure | Status Epilepticus |
|------------------------------|---|--|---|
| 0.5 to 2 mg SL or SC Q4H PRN | 1 to 2 mg SL or SC stat then 1 to 2 mg Q4H to Q6H | 4 to 8 mg IV or SC stat, then 2 to 4 mg Q4H to Q6H | 2 to 8 mg IV, SC or SL stat, then q10min to q20min until controlled |

Management for Specific Symptoms Outlined in this Guideline

1) Twitching or Myoclonus Management

-  Stop the offending drug, whenever possible.^{12, 24, 25} Often myoclonus gradually resolves in a few days.^{2, 12, 24} Some medications require a gradually tapering to prevent complications, e.g., cardiovascular and central nervous system (CNS).²⁶
-  Reduce the dose of the offending drug.¹ Reduce opioid dose by 20-30%¹¹ or 30-50% for high doses,²⁸ and reduce dosing interval as well with irreversible renal failure for renally excreted opioids.¹³
-  The benefit of a dose reduction over rotation may be less certain and only postpone the need to switch opioids.²⁵
-  Do not use naloxone to treat opioid-induced myoclonus as it will not respond and may reverse symptom control for other symptoms.^{1, 10, 25, 27}
-  Stop other non-essential medications.⁶
-  Switch (rotate) to a different opioid. If hyperalgesia accompanies the myoclonus, a switch is particularly helpful.²⁴
-  Fentanyl or methadone are useful choices for experienced prescribers as both of these have minimal or no active neurotoxic metabolites.^{1, 10, 24}
-  Maintain patient pain and symptom goals. Do not solely reduce opioid to control myoclonus.²⁴
-  Consider use of non-opioid adjuvant analgesics, e.g., anticonvulsants, acetaminophen, and others.²⁹ Refer to Pain Management guideline.
-  Treat pharmacologically to resolve reversible causative metabolic abnormalities.
-  As evidence and topic management guidelines are not robust,³⁰ utilize further resources including palliative care physician consultants, medical specialists, or experienced multidisciplinary clinicians including clinical pharmacists.

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2) Twitching or Myoclonus Drug Dosing

-  Choice of second-line anticonvulsants for management is uncertain. Benzodiazepines are commonly selected, in part based on suitability for patient setting, ease of administration, cost and familiarity. Options include:
 -  Midazolam, 1 to 5 mg IV, SC, buccal PRN (especially in uremic-induced).²⁰
 -  Clonazepam, starting at 0.5 mg orally once or twice daily.^{13, 31}

3) Seizure Management

-  Avoid starting anticonvulsants prophylaxis in brain tumor patients (primary or metastatic) if the patient has never had any seizures, due to lack of benefit and risk of drug burden.^{2, 21}
-  Initiation of long-term anticonvulsants after a first time seizure may not be required.^{8, 23}
-  Assess and provide treatment if high risk of reoccurrence, e.g., in brain metastases from melanoma, choriocarcinoma, renal cell carcinoma or thyroid papillary cancer.²¹
-  Review the current dose of corticosteroid; consider starting one adjunctively in those with intracranial tumour and seizure or scheduled cerebral radiotherapy.²³

4) Seizure Drug Dosing

-  Review individual seizure type and tailor monotherapy anticonvulsant to patient.²⁷
-  Midazolam via continuous subcutaneous infusion over 24 hours can be used²³; however, review use and suitability with local palliative care team.

5) Status Epilepticus Management

-  Status epilepticus should be controlled even in the unconscious patient near death because of the distress that continuous seizures cause to the patient's family.³
-  First line: Lorazepam 2 to 8 mg IV or SC or SL STAT then q10 to 20 min until controlled. IV maximum infusion rate 2 mg per minute.³
-  Alternatively: Midazolam 5 to 10 mg IV, buccally, or Diazepam 10 to 20 mg IV or rectally.^{3, 27}
-  Phenytoin 50 mg per min IV until seizure stops or maximum 20mg per kg per 24 hours.³
-  Valproic acid loading dose 20 mg per kg then 3 to 5 mg per kg per min infusion.³
-  Failing control: Phenobarbital 120 mg SC or IV and titrating to control.³

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-  **Myoclonus** is described as brief muscle jerks or spasms. They may appear before or during sleep. While common, they rarely need treatment. Help family members differentiate between myoclonus and seizure activity:
 -  Increased frequency or intensity may indicate an underlying problem; instruct patient and family to inform the care team of any changes.
-  **Seizures** are frightening to the patient and family. Take time afterward to explore concerns of the patient and family, and offer honest reassurance.²³ Address questions,^{3,16} dispel fears and maximize comfort.
-  Primary focus is on safety during and after seizures, medication use, eliminating the underlying cause if feasible and knowing when to contact the health care provider.¹⁵
-  Ensure alternate medication routes have been made available if needed and instruct patient's family on how to provide medication for active management.⁸
-  Do not attempt to restrain the person; loosen tight clothing around the neck.
-  Do not shout at the person or expect verbal commands to be obeyed.
-  Do not try to force anything into the patient's mouth. Do not give any fluids or food by mouth until the person has fully recovered consciousness.
-  When the seizure stops, turn the person onto his/her side until fully alert. Expect a period of sleepiness after the seizure.
-  If the patient has been driving or operating machinery, they may not continue until cleared by a physician.
-  Contact your health care provider for additional support if needed (during office hours).
-  Call after hours **Nurse Line** if available in your region, as needed.

ADDITIONAL RESOURCES FOR MANAGEMENT OF SEIZURES

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Resources Specific to Seizures

- B.C. Epilepsy Society: information sheets on safety during seizures, diary templates, emotional support etc.
→ <http://www.bcepilepsy.com/resources/information-sheets>
- BC Cancer Agency: Brain and central nervous system cancer
→ <http://www.bccancer.bc.ca/health-info/types-of-cancer/brain-central-nervous-system>
- BC Cancer Agency: Headlines: a newsletter for brain tumor patients and their families
→ <http://www.bccancer.bc.ca/health-info/types-of-cancer/brain-central-nervous-system/headlines>

General Resources

- **Provincial Palliative Care Line** – for **physician** advice or support, call **1 877 711-5757** In ongoing partnership with the Doctors of BC, the toll-free Provincial Palliative Care Consultation Phone Line is staffed by Vancouver Home Hospice Palliative Care physicians 24 hours per day, 7 days per week to assist physicians in B.C. with advice about symptom management, psychosocial issues, or difficult end-of-life decision making.
- BC Centre for Palliative Care: Serious Illness Conversation Guide
→ <http://www.bc-cpc.ca/cpc/>
- BC Guidelines: Palliative Care for the Patient with Incurable Cancer or Advanced Disease
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care>
- BC Palliative Care Benefits: Information for prescribers
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program>
- National Centre for Complementary and Alternative Medicine (NCCAM) for additional information on the use of non-pharmacological interventions
→ <https://nccih.nih.gov/>
- Canadian Association of Psychosocial Oncology: Pan-Canadian Practice Guideline: Screening, Assessment and Management of Psychosocial Distress, Depression and Anxiety in Adults with Cancer
→ http://www.capo.ca/wp-content/uploads/2015/11/FINAL_Distress_Guideline1.pdf
- Fraser Health psychosocial care guideline
→ <https://www.fraserhealth.ca/media/psychosocial%20care.pdf>

Resources specific to health organization/region

- Fraser Health
→ <http://www.fraserhealth.ca/health-professionals/professional-resources/hospice-palliative-care/>

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- First Nations Health Authority
→ <http://www.fnha.ca/>
- Interior Health
→ <https://www.interiorhealth.ca/YourCare/PalliativeCare/Pages/default.aspx>
- Island Health
→ http://www.viha.ca/pal_eol/
- Northern Health
→ <https://www.northernhealth.ca/Professionals/PalliativeCareEndofLifeCare.aspx>
- Providence Health
→ <http://hpc.providencehealthcare.org/>
- Vancouver Coastal Health
→ <http://www.vch.ca/your-care/home-community-care/care-options/hospice-palliative-care>

Resources specific to patient population

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians
→ <https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf>
- ALS Society of British Columbia 1-800-708-3228
→ www.alsbc.ca
- BC Cancer Agency: Symptom management guidelines
→ <http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management>
- BC Renal Agency: Conservative care pathway and symptom management
→ <http://www.bcrenalagency.ca/health-professionals/clinical-resources/palliative-care>
- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management
→ <http://www.bcheartfailure.ca/for-bc-healthcare-providers/end-of-life-tools/>
- Canuck Place Children's Hospice
→ <https://www.canuckplace.org/resources/for-health-professionals/>
 - 24 hr line – 1.877.882.2288
 - Page a Pediatric Palliative care physician – 1-604-875-2161 (request palliative physician on call)
- Together for short lives: Basic symptom control in pediatric palliative care
→ http://www.togetherforshortlives.org.uk/professionals/resources/2434_basic_symptom_control_in_paediatric_palliative_care_free_download

UNDERLYING CAUSES OF TWITCHING, MYOCLONUS AND SEIZURES

Information on underlying causes contained within the body of the document.

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MEDICATIONS FOR MANAGEMENT OF TWITCHING, MYOCLONUS AND SEIZURES

Information on medications for management contained within the body of the document.

Prices for prescription drugs may be obtained from BC PharmaCare. The British Columbia Palliative Care Benefits Plan <http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/palliative-formulary.pdf> provides province wide drug coverage for many of the recommended medications—check website to confirm coverage. **Consider price when choosing similarly beneficial medications, especially when the patient / family is covering the cost.**

TWITCHING, MYOCLONUS AND SEIZURES MANAGEMENT ALGORITHM

No management algorithm included in this document.

TWITCHING, MYOCLONUS AND SEIZURES EXTRA RESOURCES OR ASSESSMENT TOOLS

No extra resources or assessment tools included in this document.

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DEFINITION

Delirium is a syndrome of abrupt onset and fluctuating disturbance in attention and awareness that is a decline from baseline status.¹⁻³ It is typified by cognitive dysfunction along with changes in psychomotor behaviour, mood, and sleep-wake cycle.⁴⁻⁶ It may include hallucinations. Avoid the use of overlapping terms such as ‘confusion’, ‘acute confusional state’, ‘terminal or pre-terminal restlessness’ to prevent miscommunication.⁷ Delirium has three subtypes, all of which occur in palliative care⁸⁻¹¹:

- **Hyperactive - 30%** (restless and agitated; hallucinations more common): most often identified.¹² May be misinterpreted as pain leading to administration of higher drug doses, which then could increase delirium.¹³
- **Hypoactive - 48%** (drowsy and withdrawn): most prevalent, yet most often missed, dismissed as “normal dying”, or misdiagnosed as fatigue or depression; it also has highest mortality.^{4, 14}
- **Mixed subtypes – 22%**: fluctuates between both.¹⁵⁻¹⁷

PREVALENCE

Delirium is common in palliative care. It occurs in 20-88% of cancer patients.^{1,6,7} Although delirium often occurs 24 to 48 hours before death, it is not a “normal” part of dying.¹¹ In some cases, subtle signs up to 7 days prior,^{10, 17-19} when identified, may enable reversal of symptoms, allowing for a peaceful death.²⁰

IMPACT

Delirium is a poor prognostic indicator²¹ and often predicts death within days to weeks.²²⁻²⁵ Regardless of subtype, delirium is distressing to patients, families, and healthcare providers, impairing quality of living and quality of dying.^{1, 7, 10, 26, 27} It interferes with identification of other symptoms, is associated with increased falls, pressure sores and greater hospitalization, morbidity and mortality.⁶ It may result in shocking behaviours,²⁷ prolonged grief, and impaired opportunity for closure at end of life.²⁰ Prompt recognition and treatment is essential in order to improve patient and family outcomes, especially in the final stages of an illness.¹⁰

STANDARD OF CARE

Step 1 | Goals of care conversation

Determine goals of care in conversation with the patient, family and interdisciplinary team. Refer to additional resources ([Additional resources for management of delirium](#)) for tools to guide conversations and required documentation. Goals of care may change over time and need to be reconsidered at times of transition, e.g., disease progression or transfer to another care setting.

Step 2 | Assessment

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Identify predisposing factors which increase vulnerability and risk for delirium: age over 65 years, dementia, visual or hearing impairment, immobility, functional dependence, malnutrition, substance use, multiple chronic co-morbidities, multiple medications, admission to hospital.^{6, 26, 28} Restraints increase risk of delirium by 3 times.^{29, 30} Screen high risk patients routinely.³¹

Signs and Symptoms of Delirium may include⁶:

- Acute onset.
- Fluctuating over the course of a day.
- Attention disturbance; restlessness.
- Altered reasoning/rambling thinking.
- Agitated, angry, emotionally labile, depression, lethargy.
- Disorientation to: time, person and place.
- Sleep-wake cycle disturbance.
- Memory impairment.
- Hallucinations – visual; nightmares.
- Language fluency disturbance.
- Myoclonus, miosis, seizures, tremors (opioid neuro-toxicity) – specific symptoms.
- Tachypnea (sepsis, hypoxemia, central processes) – specific symptoms.

Step 2 | Assessment continued on [next page](#)

Delirium Assessment: Using Mnemonic O, P, Q, R, S, T, U and V⁹

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| Mnemonic Letter | Assessment Questions <i>Whenever possible, ask the patient directly; however, it is essential to include family and caregivers in the interview as the patient may be unable to cooperate or communicate effectively.</i> |
|-------------------------------|---|
| O nset | When did it begin? How long does it last? How often does it occur? |
| P rovoking /Palliating | What brings it on? What makes it better? What makes it worse? |
| Q uality | What does it feel like? Can you describe it? Do you feel confused? Are you seeing or hearing anything unusual? How are you sleeping? |
| R egion/Radiation | Not applicable |
| S everity | How bothered are you by this symptom? What would you rate it on a scale of 0-10 (0 being none and 10 being the worst possible)? Right now? At worst? On average? Are there any other symptom(s) that accompany this symptom? Do you know what day/month/year it is? Do you know where you are right now? Can you tell me your full name? |
| T reatment | What medications and treatments are you currently using? Are you using any non-prescription treatments, herbal remedies, or traditional healing practices? How effective are these? Do you have any side effects from the medications and treatments? What have you tried in the past? Do you have concerns about side effects or cost of treatments? |
| U nderstanding | What do you believe is causing this symptom? How is it affecting you and/or your family? What is most concerning to you? |
| V alues | What overall goals do we need to keep in mind as we manage this symptom? What is your acceptable level for this symptom (0-10)? Are there any beliefs, views or feelings about this symptom that are important to you and your family? |

Symptom Assessment: Physical assessment as appropriate for symptom

Conduct history and physical, review medications and doses, medical/surgical, psychosocial and physical environment.⁹

Diagnostics: consider goals of care before ordering diagnostic testing

Lab tests include: CBC, electrolytes, calcium, albumin, glucose, renal, liver and thyroid function, urinalysis, pulse oximetry, chest x-ray. Also do ECG, cultures, and brain imaging as appropriate.^{9, 32} Consider prior function, disease trajectory, and goals of care to determine the extent of investigation.^{4, 6, 19, 20, 26, 33}

Specific diagnostic tools

(See [Delirium extra resources or assessment tools](#))

- DSM-V^{1, 7, 10}
- Differentiating the 3 D's

Step 3 | Determine possible causes and reverse as possible if in keeping with goals of care (For more details, see [Underlying causes of delirium in palliative care](#))

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Common causes (See [Underlying causes of delirium in palliative care](#)) are often multi-factorial and may include^{6, 9, 34-36}:

- Infection, metabolic disturbance, hypoxia, organ failure, medications
- Withdrawal from alcohol, illicit drugs, benzodiazepines
- Pain, constipation, dehydration, retention, urinary catheters, sleep deprivation
- New/unfamiliar environments, psychosocial, psychiatric⁹

Identification and management of underlying causes will resolve 30-50% of palliative delirium episodes. However, in final days, reversibility reduces to between 10-15%.^{37, 38} Major organ failure and hypoxic encephalopathy are not reversible.³⁹ The most reversible factors include drug effects (e.g., opioid neurotoxicity), electrolyte disturbances, and physical discomfort.⁴⁰

PRINCIPLES OF MANAGEMENT



When considering a management approach, always balance burden of a possible intervention against the likely benefit (e.g., does the intervention require transfer to another care setting?)

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- Screen all high risk patients routinely and regularly using standardized tools.⁸
- Involve interdisciplinary team, patient, family²⁰ and volunteers. Use preventative measures to minimize exposure to known risks.^{1, 41, 42}
- Provide patient and family education to prevent, normalize, manage and reduce distress of delirium episodes.^{1, 8, 20, 27} Ensure holistic perspective includes psychosocial, spiritual and cultural care.
- **Identify and treat reversible underlying causes.**^{6-8, 26}
- **Ensure use of non-pharmacological approaches.**^{8, 19, 43, 44}
- Manage distressing symptoms with caution, using the lowest effective doses of least harmful agent.²⁶
- For severe distress or if behaviour creates a safety risk for patient or others: consult Palliative Specialist. Ensure methods are aligned with patient goals^{8, 9, 26} and disease trajectory for management of the symptom and/or sedation.^{45, 46}

Step 4 | Interventions

LEGEND FOR USE OF BULLETS

Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence, using a modified GRADE process.

| | |
|--|--|
|  | Use with confidence: recommendations are supported by moderate to high levels of empirical evidence. |
|  | Use if benefits outweigh potential harm: recommendations are supported by clinical practice experience, anecdotal, observational or case study evidence providing low level empirical evidence. |
|  | Use with caution: Evidence for recommendations is conflicting or insufficient, requiring further study |
|  | Not recommended: high level empirical evidence of no benefit or potential harm |

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Non-pharmacological interventions: Use for all levels and types of delirium

It may be possible to manage delirium in the home or residential care facility with appropriate planning and support for the patient, family and staff; all of these interventions do not necessarily require additional equipment or admission to acute care.

-  **Utilize non-pharmacological interventions preferentially** as they provide greater evidence of benefit, without harm, than medications for mild to moderate delirium.^{5, 42-44, 51}
-  **Use multicomponent strategies** as in Hospital Elder Life Program (**HELP** – see [Additional resources for management of delirium for link](#)): frequent reorientation and mentally engaging activities for cognitive impairment; mobilization support; hearing aids and eyeglasses; adequate oral hydration, and sleep hygiene reduce risk for delirium (33-40%) and falls (57%) in older hospital patients.^{8, 41, 52-54}
-  **Promote one-to-one observation** to maintain safety, reduce fear, and support re-orientation.⁶
-  Prevent over-stimulation; keep visitors/staff changes to a minimum.⁹
-  Promote massage, relaxation therapy, exercise,⁵⁵ and rehabilitation therapy.^{1, 5, 56}
-  Avoid immobility, indwelling catheters, intravenous lines or equipment that impedes mobility.^{9, 26}
-  Consider parental hydration in time-limited trial if appropriate for patient trajectory and goals of care. Stop if adverse effects or no benefit as little evidence of effectiveness.^{57, 58}
-  Physical restraints increase risk of delirium.⁵⁹

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Scrutinize medication profile to identify drug causes of delirium. Pharmacist assistance can be invaluable.⁶⁰

 Neuroleptic/antipsychotic drugs are sometimes required in addition to non-pharmacologic interventions. Use the lowest effective dosage which is proportionate to the severity of delirium to maximize safety and dignity. There is still many questions regarding which drugs are most appropriate.⁴³

 Consider a switch of opioid, the tapering/discontinuation of benzodiazepines, and tapering of corticosteroid dose.⁶⁰

Antipsychotic role is unclear, lacking established evidence of benefit without harm.^{43, 61}

 Use is off-label; no Canadian drugs are approved for delirium prevention or treatment.

 Antipsychotic risks may be a class effect; differences are unsubstantiated.⁴³

 Clinicians' own distress may result in inappropriate antipsychotic use.^{62, 63}

 Harm (distress worsened, greater EPS) occurred at low doses within 72 hours.¹⁰

Avoid use of

 Haloperidol^{10, 64-66} and risperidone for treatment of **mild** delirium in palliative patients.^{43, 67}

 Medications to prevent delirium; effectiveness is not established.^{14, 68}

 Opioids to treat delirium as they have no anti-agitation actions. New or increased doses of opioids may potentially worsen, if no change in pain.⁶⁹

 Cholinesterase inhibitors to treat delirium, e.g., rivastigmine or donepezil.^{10, 14, 60}

 Other drugs suggested to possibly play a treatment role but, as yet, lack adequate evidence, including methylphenidate, melatonin, trazodone.^{14, 70, 71}

Benzodiazepines

 Use is supported for delirium only when cause is alcohol⁷² or sedative drug withdrawal.¹⁰

 Are causes of delirium, confusion, paradoxical reactions, over sedation, ataxia, falls.^{10, 73}

 May be used in palliative sedation to reduce seizure risk, myoclonus, muscle tension, or acute agitation crisis.⁶⁹

 Have not been shown to hasten death in advanced illness.^{69, 74}

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When delirium is moderate to severe, unmanageable, poses concerns of harm to self/caregivers, and/or is causing distress to the patient and family

- ⚠ Haloperidol is considered first-line therapy, although there is a lack of established dose range^{17, 43, 73, 75} and a recent study has suggested it may require further investigation.⁴³ Starting dose of 0.5 mg (0.25 mg for elderly) to 2 mg SC, IV or PO Q1H until calming occurs, then Q4-6H for severe delirium.⁷⁷
- ⚠ Methotrimeprazine is a more sedating alternative to haloperidol; dosing 12.5 to 25 mg SC, IV or PO Q1-2H until calming occurs, then Q6-8H.⁷⁸
- ⚠ Additionally, for temporary sedation, in discussion with a palliative specialist, consider non-antipsychotics such as midazolam 2.5 to 5 mg SC or IV PRN; avoid oversedation.^{69, 76}
- ⚠ **Specialist consultation is recommended for severe delirium to consider drug therapy risk/benefit, delirium reversibility, and appropriate management options.** This may include palliative sedation.

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-  Provide anticipatory guidance on what to expect. Normalize to reduce distress.
-  Provide guidance on how to interact with patient: gentle reassurance, not to argue, use of a calm voice and presence.
-  Sometimes patients may act out of character which can cause distress to the family. Explain that delirium symptoms are due to illness, are common, and can fluctuate.
-  Explain that delirium becomes less reversible near end of life.
-  Some patients experience the presence of deceased loved ones, angels, spirits or others, either by seeing them, hearing their voice or sensing they are near. Be careful about interpreting this as a delirious hallucination as it may be connected to spiritual or cultural beliefs and could be comforting to the patient and family.

Teach family to use non-pharmacological interventions

-  Promote calm, re-orienting environment (clocks, calendar) and familiar objects in room. Encourage cognitively stimulating activities and mobility, if patient able.
-  Ensure hearing aids and glasses are available/functioning.
-  Offer small amount of preferred food and fluids frequently.
-  Facilitate sleep: relaxation music at bedtime, warm drinks and gentle massage; avoid waking patients from sleep; use night light.
-  Provide comfort and re-orientation with presence of family or well-known friend.
-  Teach family to watch for confusion that worsens in evening (sun-downing). This may be the first sign of delirium.
-  Contact healthcare provider if patient distress or safety concerns.

ADDITIONAL RESOURCES FOR MANAGEMENT OF DELIRIUM

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Resources specific to delirium

- BC Guidelines: Delirium
→ http://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/palliative2_delirium.pdf
- Canadian Coalition for Seniors' Mental Health. Guideline on the assessment and treatment of delirium in older adults at the end of life. Adapted from the CCSMH National guidelines for seniors' mental health. The assessment and treatment of delirium. Toronto: CCSMH, 2010.
→ <http://www.health.gov.bc.ca/library/publications/year/2012/bpsd-guideline.pdf>
- Yale University School of Medicine: HELP – Hospital Elder Life Program
→ <http://www.hospitalelderlifeprogram.org/>

General Resources

- **Provincial Palliative Care Line** – for **physician** advice or support, call **1 877 711-5757** In ongoing partnership with the Doctors of BC, the toll-free Provincial Palliative Care Consultation Phone Line is staffed by Vancouver Home Hospice Palliative Care physicians 24 hours per day, 7 days per week to assist physicians in B.C. with advice about symptom management, psychosocial issues, or difficult end-of-life decision making.
- BC Centre for Palliative Care: Serious Illness Conversation Guide
→ <http://www.bc-cpc.ca/cpc/>
- BC Guidelines: Palliative Care for the Patient with Incurable Cancer or Advanced Disease
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care>
- BC Palliative Care Benefits: Information for prescribers
→ <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program>
- National Centre for Complementary and Alternative Medicine (NCCAM) for additional information on the use of non-pharmacological interventions
→ <https://nccih.nih.gov/>
- Canadian Association of Psychosocial Oncology: Pan-Canadian Practice Guideline: Screening, Assessment and Management of Psychosocial Distress, Depression and Anxiety in Adults with Cancer
→ http://www.capo.ca/wp-content/uploads/2015/11/FINAL_Distress_Guideline1.pdf
- Fraser Health psychosocial care guideline
→ <https://www.fraserhealth.ca/media/psychosocial%20care.pdf>

Resources specific to health organization/region

- Fraser Health
→ <http://www.fraserhealth.ca/health-professionals/professional-resources/hospice-palliative-care/>

Additional resources for management of delirium continued on [next page](#)

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- First Nations Health Authority
→ <http://www.fnha.ca/>
- Interior Health
→ <https://www.interiorhealth.ca/YourCare/PalliativeCare/Pages/default.aspx>
- Island Health
→ http://www.viha.ca/pal_eol/
- Northern Health
→ <https://www.northernhealth.ca/Professionals/PalliativeCareEndofLifeCare.aspx>
- Providence Health
→ <http://hpc.providencehealthcare.org/>
- Vancouver Coastal Health
→ <http://www.vch.ca/your-care/home-community-care/care-options/hospice-palliative-care>

Resources specific to patient population

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians
→ <https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf>
- ALS Society of British Columbia 1-800-708-3228
→ www.alsbc.ca
- BC Cancer Agency: Symptom management guidelines
→ <http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management>
- BC Renal Agency: Conservative care pathway and symptom management
→ <http://www.bcrenalagency.ca/health-professionals/clinical-resources/palliative-care>
- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management
→ <http://www.bcheartfailure.ca/for-bc-healthcare-providers/end-of-life-tools/>
- Canuck Place Children's Hospice
→ <https://www.canuckplace.org/resources/for-health-professionals/>
 - 24 hr line – 1.877.882.2288
 - Page a Pediatric Palliative care physician – 1-604-875-2161 (request palliative physician on call)
- Together for short lives: Basic symptom control in pediatric palliative care
→ http://www.togetherforshortlives.org.uk/professionals/resources/2434_basic_symptom_control_in_paediatric_palliative_care_free_download

UNDERLYING CAUSES OF DELIRIUM IN PALLIATIVE CARE^{37, 78, 80-82}

Causes for delirium are usually multi-factorial.

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| Potentially Reversible Causes of Delirium | Contributing Factors |
|--|---|
| Neoplastic/structural abnormalities | <ul style="list-style-type: none"> Primary tumor of brain,^{80, 81, 83} Metastases^{80, 81, 83, 84} Tumor burden or location⁴⁵ Subdural hematoma, Stroke⁴⁵ |
| Infection/inflammation | <ul style="list-style-type: none"> Pneumonia, urinary tract infection,^{45, 80, 83-91} cellulitis, other causes of sepsis⁷⁸ |
| Metabolic | <ul style="list-style-type: none"> hypercalcemia, uremia, hypoglycemia, hyperglycemia, or hyponatremia^{45, 81, 83-85, 87, 89, 91} |
| General discomfort | <ul style="list-style-type: none"> pain, constipation, urinary retention, or dehydration^{80, 81, 83-85, 89, 90, 92} |
| Drug effects ^{69,93, 94, 95} Micromedex Drug List ^{3, 96} | <ul style="list-style-type: none"> Antibiotics ; Anticholinergic drug^{80, 81, 83} Anticonvulsants⁸⁸; Antidepressants; Antiemetics^{80, 83} Antifungals; Antihistamines; Antihypertensives^{80, 83} Antipsychotics⁴⁵; Antivirals^{80, 83, 89,82, 97, 98} Cardiovascular; Chemotherapy^{81, 83, 88} Corticosteroids⁸⁴; Dopamine Agonists H₂ antagonists^{45, 80, 83, 84, 88}; herbals (St. John's Wart) Hypnotics, sedatives – benzodiazepines*; muscle relaxants NSAIDs; Opioids*^{45, 81, 98} |
| Over dosage due to: | <ul style="list-style-type: none"> Physical deterioration⁴⁵ Metabolic causes^{45, 84} Accidental^{45, 83, 85}; Intentional – alcohol abuse^{45, 88} |
| Drug withdrawal from: | <ul style="list-style-type: none"> Alcohol⁹⁹ Barbiturates Benzodiazepines^{45, 88} Nicotine⁴⁵ Opioids^{80, 83, 84, 86} Corticosteroids^{80, 84} |
| Cardio-pulmonary | <ul style="list-style-type: none"> Cerebral hypoxia, hypercapnia, cerebrovascular disease^{45, 91} |
| Endocrine dysfunction | <ul style="list-style-type: none"> Thyroid and adrenal^{80, 83, 84, 88, 89} |
| Organ dysfunction/failure | <ul style="list-style-type: none"> Liver^{80, 81, 87, 88} Renal^{81, 83, 84, 92, 98} |
| Malnutrition | <ul style="list-style-type: none"> Thiamine or folate/B₁₂^{45, 80, 84-86, 89} |
| Trauma | <ul style="list-style-type: none"> Convulsion, subdural hematoma, or hemorrhage^{45, 83-86, 88} |
| Psychosocial/psychiatric | <ul style="list-style-type: none"> Grief⁸⁸ Sensory deprivation¹⁰⁰ or overload¹⁰⁰ Social isolation¹⁰⁰ Visual or Hearing Impairment/Linguistic Barriers |
| Imminently dying | <ul style="list-style-type: none"> Any combination of above⁷⁸ |

Note: Drug-induced causative studies within palliative patients are scarce; however, within other patients, delirium risk is most associated with **opioids and benzodiazepines**³ and should be highly presumed as causative.

All medications should be examined, in part as secondary and contributory drug interactions could be impactful.

MEDICATIONS FOR MANAGEMENT OF DELIRIUM

Information regarding medication is contained in the body of this document

Prices for prescription drugs may be obtained from BC PharmaCare. The British Columbia Palliative Care Benefits Plan <http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/palliative-formulary.pdf> provides province wide drug coverage for many of the recommended medications—check website to confirm coverage. **Consider price when choosing similarly beneficial medications, especially when the patient / family is covering the cost.**

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DELIRIUM MANAGEMENT ALGORITHM

No management algorithm included in this document.

DELIRIUM EXTRA RESOURCES OR ASSESSMENT TOOLS

Confusion Assessment Method to assess for delirium; CAM/PRISME chart used with permission from Interior Health.^{46, 102}

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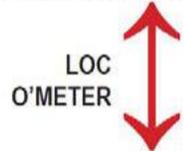
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Directions: Initiate CAM & PRISME for patients who are delirious or identified as high risk (3 or more risk factors) or show unexplained behaviors. Assess Q shift & PRN.

| 1. Use Confusion Assessment Method (CAM) assess for delirium | | | | | | | | | | | |
|---|--|---|---|--|--|---------------------------|---|---|--|-----------------------------------|---|
| CAM | <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 30%; padding: 5px;">1. ACUTE ONSET AND FLUCTUATING COURSE</td> <td style="padding: 5px;"> Does the abnormal behavior: <ul style="list-style-type: none"> • come and go? • increase/decrease in severity? </td> </tr> <tr> <td style="padding: 5px;">2. INATTENTION</td> <td style="padding: 5px;"> Does the patient: <ul style="list-style-type: none"> • have difficulty focusing attention? • become easily distracted? • have difficulty following a conversation? </td> </tr> <tr> <td style="padding: 5px;">3. DISORGANIZED THINKING</td> <td style="padding: 5px;"> <table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none;"> Is the patients' thinking <ul style="list-style-type: none"> • disorganized? • incoherent? </td> <td style="width: 50%; border: none;"> Does the patient have: <ul style="list-style-type: none"> • rambling speech? • Illogical flow of ideas? </td> </tr> </table> </td> </tr> <tr> <td style="padding: 5px;">4. ALTERED LEVEL OF CONSCIOUSNESS</td> <td style="padding: 5px;"> What is the patient's level of consciousness? <ul style="list-style-type: none"> • Vigilant (hyperalert) • Alert (normal) • Lethargic (drowsy, easy to arouse) • Stupor (difficult to arouse) • Coma (completely unarousable) </td> </tr> </table> | 1. ACUTE ONSET AND FLUCTUATING COURSE | Does the abnormal behavior: <ul style="list-style-type: none"> • come and go? • increase/decrease in severity? | 2. INATTENTION | Does the patient: <ul style="list-style-type: none"> • have difficulty focusing attention? • become easily distracted? • have difficulty following a conversation? | 3. DISORGANIZED THINKING | <table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none;"> Is the patients' thinking <ul style="list-style-type: none"> • disorganized? • incoherent? </td> <td style="width: 50%; border: none;"> Does the patient have: <ul style="list-style-type: none"> • rambling speech? • Illogical flow of ideas? </td> </tr> </table> | Is the patients' thinking <ul style="list-style-type: none"> • disorganized? • incoherent? | Does the patient have: <ul style="list-style-type: none"> • rambling speech? • Illogical flow of ideas? | 4. ALTERED LEVEL OF CONSCIOUSNESS | What is the patient's level of consciousness? <ul style="list-style-type: none"> • Vigilant (hyperalert) • Alert (normal) • Lethargic (drowsy, easy to arouse) • Stupor (difficult to arouse) • Coma (completely unarousable) |
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|  | | | | | | | | | | | |
| KEY: Presence of features 1& 2 plus either 3 &/or 4 is positive for delirium | | | | | | | | | | | |
| 2. Use PRISME to identify & address physiological, psychosocial & environmental factors | | | | | | | | | | | |
| PR | <table style="width: 100%; border: none;"> <tr> <td style="width: 30%; border: none;">PAIN</td> <td style="border: none;"> <ul style="list-style-type: none"> • Provide regular analgesia & nonpharmacological methods. Reassess pain control Q shift, especially with movement. </td> </tr> <tr> <td style="border: none;">PSYCHOSOCIAL</td> <td style="border: none;"> <ul style="list-style-type: none"> • Assess mental health, dementia & ability to cope with stress/stimuli </td> </tr> </table> | PAIN | <ul style="list-style-type: none"> • Provide regular analgesia & nonpharmacological methods. Reassess pain control Q shift, especially with movement. | PSYCHOSOCIAL | <ul style="list-style-type: none"> • Assess mental health, dementia & ability to cope with stress/stimuli | | | | | | |
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| R | <table style="width: 100%; border: none;"> <tr> <td style="width: 30%; border: none;">RESTRAINT</td> <td style="border: none;"> <ul style="list-style-type: none"> • Avoid restraints. Use alternatives </td> </tr> <tr> <td style="border: none;">RETENTION</td> <td style="border: none;"> <ul style="list-style-type: none"> • Palpate abdomen. Bladder scan PRN. I & O catheter if essential. Remove bladder catheter ASAP. Regular toileting via commode or walking to toilet </td> </tr> </table> | RESTRAINT | <ul style="list-style-type: none"> • Avoid restraints. Use alternatives | RETENTION | <ul style="list-style-type: none"> • Palpate abdomen. Bladder scan PRN. I & O catheter if essential. Remove bladder catheter ASAP. Regular toileting via commode or walking to toilet | | | | | | |
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| I | <table style="width: 100%; border: none;"> <tr> <td style="width: 30%; border: none;">INFECTION</td> <td style="border: none;"> <ul style="list-style-type: none"> • Assess for UTI, pneumonia, C diff, purulent wound. Monitor VS. May have atypical presentation with no fever </td> </tr> <tr> <td style="border: none;">IMPACTION</td> <td style="border: none;"> <ul style="list-style-type: none"> • Determine last BM. Palpate abdomen. Rectal check PRN. Prevent & treat constipation. Bowel protocol as needed </td> </tr> <tr> <td style="border: none;">IMPAIRED COGNITION</td> <td style="border: none;"> <ul style="list-style-type: none"> • No reality orientation. Use calm, gentle approach & conversational cues to orientate patient to time & place </td> </tr> <tr> <td style="border: none;">INTAKE-ORAL</td> <td style="border: none;"> <ul style="list-style-type: none"> • Feed patient PRN. Assess dysphagia & consult OT/Dietitian PRN </td> </tr> </table> | INFECTION | <ul style="list-style-type: none"> • Assess for UTI, pneumonia, C diff, purulent wound. Monitor VS. May have atypical presentation with no fever | IMPACTION | <ul style="list-style-type: none"> • Determine last BM. Palpate abdomen. Rectal check PRN. Prevent & treat constipation. Bowel protocol as needed | IMPAIRED COGNITION | <ul style="list-style-type: none"> • No reality orientation. Use calm, gentle approach & conversational cues to orientate patient to time & place | INTAKE-ORAL | <ul style="list-style-type: none"> • Feed patient PRN. Assess dysphagia & consult OT/Dietitian PRN | | |
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| S | <table style="width: 100%; border: none;"> <tr> <td style="width: 30%; border: none;">SLEEP DISTURBANCE</td> <td style="border: none;"> <ul style="list-style-type: none"> • Ensure 4-hour sleep periods. No routine night turns. Naps OK </td> </tr> <tr> <td style="border: none;">SENSORY CHANGE</td> <td style="border: none;"> <ul style="list-style-type: none"> • Ensure glasses, hearing aids & dentures fit well and work </td> </tr> <tr> <td style="border: none;">SOCIAL ISOLATION</td> <td style="border: none;"> <ul style="list-style-type: none"> • Promote family stays & overnights PRN. Provide delirium pamphlet. Encourage familiar objects-pictures, blankets, pet visits </td> </tr> </table> | SLEEP DISTURBANCE | <ul style="list-style-type: none"> • Ensure 4-hour sleep periods. No routine night turns. Naps OK | SENSORY CHANGE | <ul style="list-style-type: none"> • Ensure glasses, hearing aids & dentures fit well and work | SOCIAL ISOLATION | <ul style="list-style-type: none"> • Promote family stays & overnights PRN. Provide delirium pamphlet. Encourage familiar objects-pictures, blankets, pet visits | | | | |
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| M | <table style="width: 100%; border: none;"> <tr> <td style="width: 30%; border: none;">MEDICATION</td> <td style="border: none;"> <ul style="list-style-type: none"> • Review recent med changes, drug levels, ETOH. Avoid medications of risk (ie, demerol, codeine, benzodiazepines) </td> </tr> <tr> <td style="border: none;">METABOLIC</td> <td style="border: none;"> <ul style="list-style-type: none"> • Evaluate fluid balance/output/labs/oxygenation. If agitated, restart IV X 2 only-consider alternatives & ensure agitation is treated </td> </tr> <tr> <td style="border: none;">MOBILITY</td> <td style="border: none;"> <ul style="list-style-type: none"> • Encourage self-care; toileting; ambulation. Up for meals </td> </tr> </table> | MEDICATION | <ul style="list-style-type: none"> • Review recent med changes, drug levels, ETOH. Avoid medications of risk (ie, demerol, codeine, benzodiazepines) | METABOLIC | <ul style="list-style-type: none"> • Evaluate fluid balance/output/labs/oxygenation. If agitated, restart IV X 2 only-consider alternatives & ensure agitation is treated | MOBILITY | <ul style="list-style-type: none"> • Encourage self-care; toileting; ambulation. Up for meals | | | | |
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| MOBILITY | <ul style="list-style-type: none"> • Encourage self-care; toileting; ambulation. Up for meals | | | | | | | | | | |
| E | <table style="width: 100%; border: none;"> <tr> <td style="width: 30%; border: none;">ENVIRONMENT</td> <td style="border: none;"> <ul style="list-style-type: none"> • Provide a quiet, supportive environment --↓ noise, lights & people • Hypoactive-Increase stimuli as tolerated. Activate • Hyperactive-Reduce stimuli, especially at night </td> </tr> </table> | ENVIRONMENT | <ul style="list-style-type: none"> • Provide a quiet, supportive environment --↓ noise, lights & people • Hypoactive-Increase stimuli as tolerated. Activate • Hyperactive-Reduce stimuli, especially at night | | | | | | | | |
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Delirium Diagnostic Criteria (DSM-V)^{7, 10}

Note: No recommended screening tools currently available; the below resource has been updated to reflect the change in DSM-V diagnostic criteria which removes level of consciousness in particular aspects of coma (**Feature D**). This remains controversial.^{6, 46}

Box 21.1 Diagnostic criteria for delirium

- A.** Disturbance in attention and awareness
- B.** The disturbance develops over a short period of time and tends to fluctuate in severity during the course of the day.
- C.** Disturbance in cognition
- D.** The disturbances in criteria A and C are not explained by another preexisting, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma.
- E.** History, physical examination, or laboratory findings indicate that the disturbance is caused by a medical condition, substance intoxication or withdrawal, or exposure to a toxin, or is because of multiple etiologies.

Source: Adapted from American Psychiatric Association (2013), reference 37.

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Occupational Therapy Cognition Toolkit ⁷⁹

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Comparison of the features of delirium, dementia and depression:

| Feature | Delirium | Dementia | Depression (includes psychotic depression) |
|--|---|--|---|
| Onset | Acute (hours to days) | Insidious (months to years) | Acute or insidious |
| Acuity | Acute illness, medical emergency | Chronic, progressive | Episodic |
| Course | Fluctuates hourly, lucid periods in a day confusion usually worsens at night | Stable throughout the day; Chronic; progresses slowly | Relatively stable; May be self-limiting, recurrent, or chronic; symptoms worse in the morning, improve during the day |
| Duration | Days to months; not always reversible | Months to years Progressive and irreversible; ends in death | Variable |
| Consciousness | Reduced; Fluctuates | Clear until late in the course of the illness | Clear |
| Hallucinations | Gross distortions, Frequent hallucinations, Usually visual or visual and auditory | Often absent in early stages; in later stages may have hallucinations, especially visual | May have hallucinations (predominantly auditory) |
| Delusions | Fleeting, poorly systematized | Often absent | May have sustained, systematized delusions |
| Attention/concentration | Impaired | Normal, except in late stages | May be disordered |
| Orientation | Usually impaired, at least for a time | Impaired as disease progresses | Selective disorientation |
| Memory | Immediate and short term memory impaired | Memory impaired, gradually worsening as disease progresses | May be selectively or minimally impaired; concerns about memory |
| Psychomotor | Increased, reduced or shifting unpredictably | Often normal | Varies from retardation to hyperactivity (in agitated depression) |
| Speech | Often incoherent; slow or rapid | Usually coherent until late stage | Normal, slow or rapid |
| Thinking | Disorganized or incoherent | Limited, impoverished and vague | Impoverished, retarded; usually organized |
| Physical illness or drug toxicity | One or both present | Often absent in Alzheimer's disease | Usually absent, but debatable |
| Affect | Variable | Variable | Depressed |
| Sleep/wake cycle | Disturbed; changes hourly | Disturbed; day/night reversal | Disturbed with early-morning waking; hypersomnia during the day |

Completed February, 2012

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