Symptom Control and Care of the Dying Patient:

Palliative Care Guidelines

7th Edition

Produced by the Kent Palliative Medicine Forum

Whilst every effort is made to ensure the accuracy of this guide, the authors and organisations supporting it cannot accept liability for inaccuracies.
Some recommendations are based on accepted practice, using medications outside their product licence, and not always with high quality evidence to support this.

Individual clinical assessment and judgement is essential.

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INTRODUCTION

This booklet is aimed at all health care professionals involved in the care of patients with incurable, progressive disease who are experiencing unpleasant symptoms. The interventions and treatments described are initial measures that all doctors and nurses should be able to start. If the symptoms do not resolve, specialist advice can be obtained from the contacts given at the end of the booklet.

Notes: cautions and contra-indications may apply to any of the medications; some of the indications are outside of the product licence, please refer to the BNF, and the Palliative care formulary
There is an increasing focus on the QT interval and drugs that prolong it. For patients with a longer prognosis or at particular risk, the Scottish palliative care guidelines mark all drugs on their site that may have this effect. (http://www.palliativecareguidelines.scot.nhs.uk/guidelines/).

DOSES

Where a range of doses is given, start at the lower end of the dose range. This should be reviewed regularly and doses increased if the symptom is not improving.

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Abbreviations

SL	Sublingual
SC	Subcutaneous
IM	Intramuscular
PO	Per oral (orally)
IV	Intravenous
CSCI	Continuous subcutaneous infusion (via a syringe driver or pump)
od	Once daily
bd	Twice daily
tds	Three times daily
qds	Four times daily
prn	As required
hr	hour
micrograms	micrograms
mg	milligrams
g	grams
mmol/l	millimoles per litre
NSAID	Non-steroidal anti-inflammatory drug
CPR	cardio-pulmonary resuscitation
ESRD	end stage renal disease
FBC	full blood count
U&Es	urea and electrolytes
LFTs	liver function tests
IVI	intravenous infusion
NGT	naso-gastric tube
GI	gastrointestinal

Management of pain

Pain is defined in a number of ways:

- Pain is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."[1]
- Pain is "what the patient says it is"[2]

This section concentrates on the pharmacological management of pain. However, pain is complex and factors other than the physical influence people's experience of pain. For pain to be managed effectively, holistic assessment and management is required. Where non-physical factors associated with pain are a prominent feature, simply adjusting analgesics will not be an effective solution to manage that person's pain. Other factors to consider when assessing and managing pain are:

Psychological
e.g. the fears and concerns of the patient, which may be associated with pain and its management or with the dying process.

Social
It is important to remember that patients are part of a wider social network. Concerns about their family, loved ones or friends may impact on their experience of pain. In addition, concerns about work and finances, loss of independence and loss of control commonly impact on people's pain experience.

Spiritual
The meaning of the illness for the patient may lead to questions about the meaning of life e.g. "why me?", "what next?"

Principles of good pain control
• Assess the patient and explore their concerns and expectations • Assess the pain, identify and treat the cause of the pain where possible. Pain may not be related to the underlying terminal diagnosis. e.g. OA • Help patients and their carers to understand symptoms • Use the analgesic ladder at the appropriate step [WHO Analgesic Ladder 1986] • Prescribe analgesia on a regular basis ("by the clock, by the mouth, by the ladder") • Prescribe appropriate analgesia for breakthrough pain • Explain the management plan to patient and carer • Review analgesic needs frequently and titrate or change medications as appropriate

Assessment

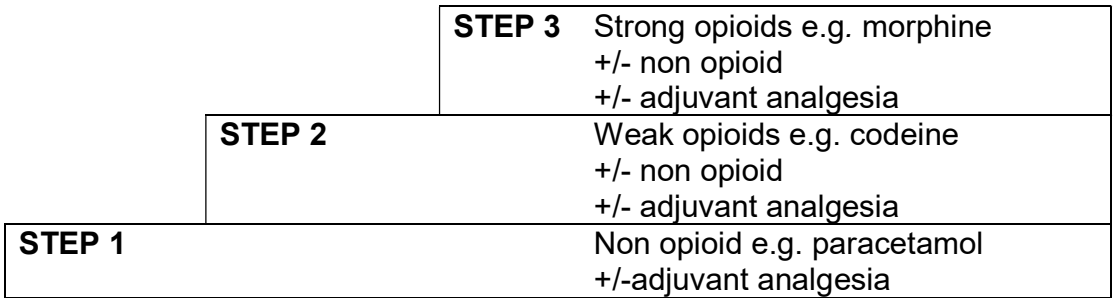
- What is the cause of the pain?
  - Does this correlate to known sites of disease/pathology?
  - Treat reversible causes.
  - Carefully exclude conditions requiring urgent intervention such as spinal cord compression, fracture, infection.
- What are the characteristics and severity of the pain?
  - Assess by the impact on activities of daily living or interference with rest / sleep.
  - Assess impact of current and previous analgesics on the severity of the pain and any side effects
- What is the **type** of pain, e.g. neuropathic, bone, visceral?
- What associated social, psychological, spiritual and physical issues are present?
- Could this be a chronic pain? If so see below page 9

Management

- All patients should be offered an explanation of what is happening, including causes of pain and rationale behind management. The holistic management of pain should also include consideration of non- drug management strategies such as relaxation techniques and complimentary therapies.
- Most patients in pain require regular analgesia, and may also require specific treatments aimed at the underlying causes (e.g. palliative radiotherapy for metastatic bone pain)
- Any patient on strong opioids should be counselled about driving. The most up to date guidance can be found on the DVLA website (www.gov.uk/drug-driving-law).

For patients who are not taking any regular analgesia:

- Start at an appropriate step of the WHO analgesic ladder (although no longer appropriate for all types of pain management, the WHO analgesic ladder remains of use in the palliative care setting).
- If pain is persisting or increasing this should prompt a step up the ladder.
- If pain is severe then it is good practice to start at step 3, i.e. strong opioids.
- Be aware that significant renal impairment (usually eGFR <30) will change your choice of analgesic, see section on renal failure (page 24).



- The usual starting doses on each step are:
  - Step 1: paracetamol 1g PO qds
  - Step 2: codeine 30mg-60mg PO qds (note steps 1 and 2 may be combined as co-codamol 30mg/500mg two tablets qds)

- Step 3: immediate release morphine 5mg-10mg every 4 hours OR modified release morphine (e.g. Zomorph capsules or MST continus tablets) 10mg-20mg every 12 hours. Refer to the opioid conversion charts p38-40.

For patients taking regular pain relief:

- Patients should usually be on only one regular opioid to avoid drug interactions
- Patients should have access to "as required" (breakthrough) analgesia, usually an opioid such as immediate release morphine (morphine oral solution or tablets) should be prescribed prn 4-hourly at a dose of 1/6th of the 24-hour oral morphine dose,
  e.g. a patient taking 90mg bd modified release morphine is taking the equivalent of 180mg oral morphine in 24 hours, therefore they should receive 30mg of immediate release morphine as required for pain 4-hourly.
- Increased use of breakthrough analgesia, e.g. more than 3 doses in a 24-hour period, should prompt a review of the regular or background dose of opioid.

Continue to titrate up the morphine dose by up to 30% every 24-48 hours until pain relief is satisfactory or adverse effects occur. If pain is not responding to opioids, then another assessment of the pain should take place and alternative approaches should be considered.

If patients are unable to take oral analgesia, then opioid analgesia should be given SC. If a patient is unable to take oral analgesia and requires regular opioid analgesia, it should be administered by continuous subcutaneous infusion (via a syringe driver).

Alternative Opioids

See opioid conversions (p38-40) for equivalence of doses.

Opioid drugs other than morphine are available and are often used for palliative care patients. Morphine remains the first choice, although there may be specific indications to use an alternative such as renal failure or intolerable adverse effects. Other opioids have differing potency and care is required when dosing. If you are not familiar with the opioid that is being prescribed, calculating the equivalent dose to oral morphine will help you to appreciate the potency of the drug and any escalation of doses required. Please seek specialist palliative care advice if needed.

Oxycodone (PO/SC)

This has a role if patients develop intolerable adverse effects from morphine and may be safer in renal impairment.

Alfentanil (SC)

This may be of use in patients with significant renal impairment (usually eGFR <30). Please contact the Palliative Care Team for further advice.

Transdermal Opioids (Patches)

These are most suitable for patients with stable analgesic requirements. They are not suitable for acute pain but may be useful for patients who:

- Are unable to take oral medication
- Are unable to comply with regular medication
- Experience intolerable adverse effects with other opioids (e.g. constipation)
- Have significantly impaired renal function

Delivery systems used by the different patch manufacturers can lead to prescribing confusion. It is now advised that when prescribing opioid patches, the brand name is used. Patches may be designed to be changed every 72hr, every 96hr or every 7-days, depending on the drug and preparation.
Due to the prolonged effect of patches, even after the patch has been removed from the skin, advice should be sought from the Palliative Care Team prior to switches between transdermal opioids and other opioids.
Ensure the patient and carers are counselled about correct usage, placement and disposal of patches (refer to BNF/pharmacist).

Fentanyl Patches (usually changed every 72 hours)
When the first patch is applied it will generally take 36-48 hours before maximal analgesic effect is achieved.
The patch strength should not be increased until it is due to be changed.
An immediate release opioid should be prescribed for breakthrough pain.
After removing a patch there will continue to be significant amounts of fentanyl acting systemically for many hours Patients who are imminently dying should have their patches continued, unless there are concerns about side effects, and additional opioid requirements should then be placed in a CSCI.

Buprenorphine Patches (TAKE CARE, depending on the preparation, these may be changed every 7 days, every 72 hours or every 96 hours)
There is a delay in onset of the analgesic effect of between 18 and 24 hours after first application of the patch and a similar delay for the effect to wear off after the patch has been removed.
An immediate release opioid should be prescribed for breakthrough pain.

Common side-effects of opioids

Constipation

Virtually all patients become constipated on regular opioids. Prescribe a regular laxative to prevent constipation, ideally a stimulant laxative. Review the dose of the laxative as the opioid dose increases [refer to page 12]. Fentanyl is the least constipating of the common strong opioids.

Nausea

May occur when starting or increasing opioids, therefore prescribe an anti-emetic for use if necessary [refer to page 13]. This often settles a few days after introduction of an opioid or an increase in dose.

Dry Mouth

This is a common side effect. Local measures can be very helpful e.g. ice cubes, sugar free chewing gum, pineapple chunks. As well as these, artificial saliva can be used (see BNF “Treatment summaries”, “Oropharynx”, “Treatment of dry mouth”). Check for oral candidiasis and treat according to local guidelines.

Drowsiness

May occur when opioids are started or the dose is increased; it is usually transient and will reduce over a few days but opioid toxicity should be excluded.

Opioid toxicity

Life threatening opioid toxicity due to respiratory depression is rare if opioids are titrated safely and according to agreed guidance. Naloxone should be used to reverse opioid toxicity if clinically significant respiratory depression is present (see p 37).

Features of non-life-threatening opioid toxicity include

- Sedation
- Confusion
- Hallucination and altered visual perceptions
- Myoclonus (this is an abnormal finding when a person is awake)

It is important to consider other reversible causes of these symptoms such as hypercalcaemia, sepsis, dehydration, renal impairment and the role of other medications.

Management of suspected non-life-threatening toxicity includes:

- address other possible causes e.g. rehydration;
- reduce opioid dose or omit next dose and review;
- opioid sparing techniques e.g. use of non-opioid analgesics;
- if considering switching opioids seek specialist advice.

N.B. When treatment for anxiety, restlessness or agitation is required this should not be achieved by increasing the opioid dose. Instead, a more specific medication should be prescribed, see guidance below.

Specific pain presentations

It may be helpful to identify the following presentations which benefit from particular management strategies:

<u>Metastatic Bone pain</u>

This is pain associated with known metastatic bone disease and is often described as a deep aching sensation over a localised point. Management should be as follows:

- Paracetamol
- NSAIDs
- Palliative radiotherapy – refer to oncology team
- Consider bisphosphonates e.g. pamidronate or zoledronate infusion (check renal function and dental status before treatment) or denosumab (this should be discussed with Oncology teams before use)
- Consider role of orthopaedic opinion if there is a risk of pathological fracture.

<u>Back pain and malignant spinal cord compression in cancer</u>

Increasing or new back pain with any neurological symptoms or signs in lower limbs or alteration in bowel or bladder function (late signs) requires urgent evaluation to exclude spinal cord compression.

- Commence dexamethasone 8mg bd immediately
- Urgent discussion with local Oncology Team
- Arrange urgent MRI of whole spine (not just the painful area)

Headache from raised intracranial pressure in cancer

May present in primary cerebral tumour or cerebral metastases. Often described as pressure, worse in the morning and on lying flat.

- Give dexamethasone, starting at 8mg bd (morning and lunchtime as may cause insomnia if given later in the day) and offer analgesia as per WHO analgesic ladder.
- If there is no response within 7 days discontinue the dexamethasone.
- If patient responds, gradually reduce the dosage to a maintenance dose. Usually decrease by 2mg every week or two weeks unless symptoms recur.
- Consider palliative radiotherapy and therefore whether further investigation is appropriate – refer to local Oncology Team

Bowel colic

Can be associated with constipation or partial intrinsic or extrinsic obstruction of the bowel. This is often described as griping and tends to come and go rather than be present constantly.

- Assess for and manage constipation.
- Consider whether the patient is at risk of bowel obstruction and requires further assessment with imaging
- Consider anti-spasmodic: hyoscine hydrobromide (as Kwells) 300microgram SL tds or hyoscine butylbromide (Buscopan) 10mg-20mg SC prn.
- In bowel obstruction, the oral route is not appropriate for drug administration (see section on intestinal obstruction).

Liver capsule pain

This is usually associated with aching pain in the right upper quadrant of the abdomen with sharp pain on movement and deep inspiration. There is usually known disease in the liver and hepatomegaly on examination.

- Paracetamol 1gram qds
- Dexamethasone 4mg-8mg od or NSAID
- Opioids can also be useful but an adjuvant e.g. pregabalin is often required to manage pain fully.

Neuropathic pain

This may be described as burning or stabbing in nature and can be associated with local paraesthesia and altered sensation.

- Follow the analgesic ladder – pain may be partly opioid responsive.
- Adjuvant analgesics:
    - Dexamethasone: 8mg od to relieve nerve compression
    - Amitriptyline: Starting dose 10mg - 25mg at night and titrate upwards OR
    - Gabapentin: Starting dose is 300mg od (elderly patients 100mg); titrate upwards as tolerated OR
    - Pregabalin: Starting dose is 75mg bd (elderly patients 25mg-50mg bd) and titrate upwards as tolerated
- TENS (Transcutaneous Electrical Nerve Stimulation): this is usually instigated by Chronic Pain Team or Physiotherapists.

Neuropathic pain may be difficult to control and advice may be needed from the Palliative Care Team.

Interventional procedures for pain

Consider referral to a pain clinic for e.g. coeliac plexus block for pancreatic pain or in difficult pain situations, when systemic analgesics are not effective and/or toxicity is problematic.

Management of persistent (chronic) pain in the palliative care setting

It has become increasingly clear that the use of the WHO analgesic ladder approach to pain management outside the arena of palliative care patients (who have incurable, progressive illness with a prognosis counted in months) carries significant risks and cannot be recommended.[3-6]

There is increasing evidence that opioids are often relatively ineffective for chronic (persistent) pain (>3 months) and moreover that their long-term use in high doses is associated with a dose dependent risk of serious harm, including problem drug use. It is strongly recommended that patients who do not achieve useful relief of pain when titrated to doses of 120mg morphine equivalent per 24 hours are referred to a specialist in pain medicine. No evidence-based argument can be made for the use of high dose opioids, i.e. 120mg morphine equivalent or more daily, in clinical practice for chronic non cancer pain.
http://www.fpm.ac.uk/faculty-of-pain-medicine/opioids-aware

Use of a syringe driver (CSCI)

The syringe driver is a battery-operated device designed to deliver drugs via a continuous subcutaneous infusion (CSCI) over 24 hours.
The main indications are the inability to swallow or absorb drugs due to:

- Weakness or coma
- Persistent nausea and vomiting
- Medical management of intestinal obstruction if surgery is not possible or appropriate

Drugs commonly used in a syringe driver

A combination of drugs can be used to achieve good symptom control.
The syringe driver site, stability of the contents and rate of infusion should be checked regularly.

Analgesics

Morphine is the most commonly used opioid analgesic used by CSCI in a syringe driver although other opioids can also be given via this route.

Calculating doses of opioid via CSCI

- Calculate the 24-hour dose of opioid on the basis of the previous 24-hour opioid requirement. Remember oral and parenteral opioid doses are not equipotent. Morphine and oxycodone are thought to be twice as potent when given by injection than when given orally. (see conversion table or access the online “Pallicalc” at http://book.pallcare.info/index.php to aid calculations).
- For breakthrough pain, prescribe 1/6th of the 24-hour opioid dose which will be the SC bolus prn injection every 2-4 hours (remember oral and parenteral opioid doses are not equipotent).

- Review the syringe driver medications every 24 hours. Review how much breakthrough medication has been required in the past 24 hours. If persistent pain or more than 3 prn doses of analgesia have been required, consider increasing the opioid in the syringe driver to take account of this.
- Remember to adjust the breakthrough opioid dose if the background opioid dose is increased or decreased so that it continues to be 1/6 of the 24-hour dose.
- Opioids are often combined with other drugs and should be diluted to an appropriate volume with water for injections or 0.9% sodium chloride.

NSAIDs

If a patient is unable to take a NSAID by mouth, an equivalent dose of diclofenac can be given by CSCI after discussion with the specialist palliative care team.

Transdermal opioids and CSCI

If setting up a CSCI via a syringe driver in a patient using transdermal patches **continue with the patch** as usual and top up the analgesic requirements with the infusion.
To calculate the dose of opioid in the syringe driver, add up how much opioid has been required for breakthrough pain in the previous 24 hours. Remember to **include the opioid dose equivalent within the patch** as well as the syringe driver when calculating the breakthrough dose of opioid [refer to Opioid Conversion Table or access the online "Pallicalc" at http://book.pallcare.info/index.php].
If pain persists seek advice from the Palliative Care Team.

Anti-emetics

Drug	Usual starting dose range/24hours
Haloperidol	1.5mg
Levomepromazine	5mg-12.5mg
Cyclizine	100mg - 150mg
Metoclopramide	30mg - 60 mg

Respiratory secretions and bowel colic

Drug	Usual starting dose range/24hours
Glycopyrronium bromide	600microgram - 1.2mg
Hyoscine butylbromide (Buscopan)	60mg- 120mg

Terminal agitation and restlessness

Drug	Usual dose range/24hours	Comments
Midazolam	10mg - 30mg	Midazolam if anxiety is predominant feature. Add levomepromazine if agitation not controlled with midazolam 60mg/24hr
Haloperidol	2.5-5mg	Antipsychotic should be used first line for hyperactive delirium.
Levomepromazine	25mg - 50mg	An alternative to Haloperidol

Higher doses can be used but if symptoms do not improve on lower doses then specialist advice should be obtained.

Seizures

If an individual is unable to take oral anti-epileptics and at high risk of seizures or seizures occur, midazolam can be used, starting with 20 -30mg over 24hours and increasing as required.
It is also possible to use levetiracetam by subcutaneous infusion (seek specialist advice).

Pre-emptive prescribing of midazolam10mg SC or IM as prn dose to be given if a seizure occurs. If uncontrolled seizures despite higher doses (>60mg midazolam/24hr) seek specialist advice.

Management of constipation

Assessment

This should include the following:

- Thorough history and examination including rectal examination; *remember that diarrhoea can be overflow from a constipated stool*.
- Medication history (to exclude potentially causative medication and to check that laxatives are co-prescribed with strong opioids) including what has worked and what hasn't.
- Exclusion of malignant bowel obstruction

Treatment

- Correct **reversible causes** and encourage fluids
- Drugs should be prescribed according to patient needs and preferences
- Oral laxatives are usually preferable to rectal interventions

Consider:

- Side-effects and contraindications
- Patient preferences
- Volume that can be tolerated

Suggested regimens

Try to avoid concurrent prescription of several different laxatives.
Titrate doses upwards every 1-2 days according to response up to maximum recommended or tolerated dose before changing to an alternative.
Consider adding a softener to a stimulant if no response after 3-4 days despite upwards titration.

STIMULANT
Senna 7.5mg-15mg usually at night and increasing as necessary.

Side effects: can cause cramps and should be avoided in bowel obstruction**.**

SOFTENER
Sodium docusate 100mg bd increasing to 200mg bd after 1-2 days according to response (stimulant effect in higher doses). Liquid docusate in unpalatable. If needing multiple capsules then a macrogol maybe more acceptable

Side effects: cramps, diarrhoea, hypokalaemia

OSMOTIC
Lactulose 15mls bd

Macrogols – available as sachets or oral solution. These may be unacceptable to very ill patients due to the volume to be ingested. Use 1 sachet or 125mls diluted oral solution od, increasing by one dose daily until effective. Maximum dose16 sachets in faecal impaction. Beware, limit to 2 sachets in patients with cardiovascular impairment.

Side-effects: Abdominal distension, pain, nausea, flatulence

RECTAL INTERVENTIONS
Suppositories e.g. Glycerol and Bisacodyl.
Bisacodyl suppositories can cause local rectal inflammation and can cause faecal leakage

Enemas e.g. Phosphate enema

In patients who have faecal impaction rectal interventions should precede oral macrogols.

OPIOID INDUCED CONSTIPATION – on specialist advice a peripherally acting opiate antagonist can be considered.

COMBINATION LAXATIVES – SPECIALIST USE ONLY
Containing softener and stimulant (e.g. Co-danthramer or Co-danthrusate)
Side-effects: cramps, diarrhoea; in immobile patients, prolonged contact with skin can cause a ‘’dantron burn’’ and excoriation. Dantron can discolour urine.

Nausea and vomiting in palliative care

Nausea and vomiting are common symptoms in palliative care occurring in over 50% of patients. There is often more than one precipitating factor making management particularly difficult.

Causes of nausea and vomiting

- Area postrema (chemoreceptor trigger zone) activity: e.g. biochemical abnormalities (raised calcium or renal failure), drug changes (opioids, cytotoxics, antibiotics, digoxin) or infection.
- Cerebral cortex activity: e.g. anxiety

- Emetic pattern generator (Vomiting centre): e.g. radiotherapy to head or neck, primary or secondary cerebral tumours
- Gastric irritation: e.g. NSAIDs, iron, cytotoxics, radiotherapy; gastric stasis or compression e.g. pressure from tumour or ascites or drug induced e.g. opioids, tricyclic antidepressants, phenothiazines, hyoscine
- Gastrointestinal obstruction.

An approach to managing nausea and vomiting

- Review current medication and discontinue any non-essential precipitating drugs
- Remove or minimise any other identified precipitating factors e.g. constipation
- Treat any reversible causes e.g. hypercalcaemia
- Choose an anti-emetic appropriate to a likely cause (see below)
- Prescribe a regular oral anti-emetic
- Consider buccal or sublingual medication if oral not tolerated
- If a patient is vomiting then an injection is necessary and if this successfully controls the vomiting, it can be followed by regular oral anti-emetics
- If the vomiting persists, commence CSCI via a syringe driver
- N.B. Reluctance to commence a syringe driver is a common reason for poor management of nausea and vomiting.

Metabolic / toxicity / drug related N&V

- Haloperidol 500microgram-1.5mg PO od at night

Raised intracranial pressure

- Cyclizine 50mg PO bd-tds

GI motility disorders without colic

- Metoclopramide 10mg PO tds-qds

Multifactorial / unknown / refractory including higher centres

- Levomepromazine 6.25mg- 12.5mg PO as a single night time dose

Possible adjuvant medication

- Lorazepam 500microgram sublingual prn may be helpful when anxiety is a precipitating factor
- Dexamethasone 4mg-16mg/day PO for raised intracranial pressure.
- Proton pump inhibitors e.g. lansoprazole 30mg PO od for gastric irritation.
- Ondansetron 4mg PO/SC but caution as constipating.

Special considerations

- Avoid centrally acting dopamine antagonists and anticholinergic drugs in Parkinson's Disease, the safest anti-emetic is domperidone
- Avoid cyclizine in severe heart failure due to tachycardia
- The prokinetic effect of metoclopramide will be lost if prescribed with an antimuscarinic drug such as cyclizine or levomepromazine.
- Avoid metoclopramide in the presence of colic as prokinetic effect will worsen pain.
- Avoid metoclopramide in patients in whom it has previously caused extrapyramidal effects and avoid long term high dose exposure wherever possible.
- Many of the antiemetic drugs prolong the QT interval – check individual drugs before prescribing if concerned.

Before moving to 2nd line treatment, consider giving a subcutaneous injection and then starting a CSCI with the relevant drug.

Management of gastrointestinal (GI) obstruction in palliative care

Symptoms/Signs indicating Malignant Bowel Obstruction

Known or suspected intra-abdominal malignancy

Alongside **one or both** of:
- Nausea or vomiting
- Colic

This may or may not be supported clinically by the following **signs:**
- Gaseous distension
- Altered bowel habit
- Tinkling bowel sounds

Confirm by abdominal X-ray or CT scan unless clinical condition makes this inappropriate or clinical diagnosis is clear.

Management plan

- Constipation excluded by digital rectal exam or radiology
- Baseline bloods to assess current status (if appropriate):
    - FBC
    - Biochemistry (U&Es, Magnesium and calcium)
    - LFTs
- MDM discussion to exclude options for surgery, stenting or chemotherapy (in malignancy) especially if good performance status, no previous surgery and isolated lesion or very chemo-sensitive disease.
- Referral to Palliative Care Team
- Consider IVI if fluid depleted or significant thirst
- Consider NGT as a temporary measure if surgery is being considered or vomiting not settling with medical management

The medical approach to managing GI obstruction differs according to the **presence or not of colic.**

For patients with no colic (unless contraindications):

- Metoclopramide 30mg-90mg/24 hours via CSCI (syringe driver)

- Trial of Dexamethasone 6.6mg SC/IV od (in the morning) with proton pump inhibitor (PPI) cover
- Oral sodium docusate 100mg-200mg bd
- Opioid at appropriate dose for tumour pain

As required medication:
- Metoclopramide for nausea 10mg SC/IV prn (limit maximum total dose 60mg/24hr)
- Opioid at appropriate breakthrough dose for tumour pain (usually one-sixth of total daily dose) SC prn 4-hourly
- Hyoscine butylbromide 10mg-20mg SC hourly with maximum of 60mg/24 hours, in case colic develops.

If colic develops switch to the following regimen:

For patients with colic
- Hyoscine butylbromide 60mg-120mg/24 hours CSCI as an antisecretory agent and antispasmodic
- Levomepromazine 5mg-25mg/24 hours CSCI as an anti-emetic
- If levomepromazine is too sedative, consider alternatives e.g. cyclizine 100mg-150mg/24 hours +/- haloperidol 500microgram-3mg/24 hours via CSCI
- Trial of dexamethasone 6.6mg SC/IV mane with PPI cover
- Oral sodium docusate 200mg bd
- Opioid at appropriate dose for tumour pain

As required medication
- Levomepromazine 2.5mg-5mg SC 6-hourly prn for nausea
- Opioid at appropriate breakthrough dose for tumour pain
- Hyoscine butylbromide 10mg-20mg SC hourly with maximum of 120mg/24 hours for colic (inclusive of dose in CSCI)

Alternative antisecretory agents or combinations can be considered, for example octreotide. Please contact Palliative Care Team for advice if this is necessary.

Acute confusional states in advanced disease

Characterised by acute onset, altered level of consciousness, fluctuating course with disorganised thinking, disorientation and inattention.

More common in the elderly, physically ill, patients in the terminal stages of their illness and patients with an underlying dementia or cerebral primary or secondary malignancy.
Whilst offering immediate treatment, consider **reversible causes**: recent drug changes, organ failure, hypoxia, infection, hypercalcaemia, dehydration, encephalopathy, hypo/hyperglycaemia.

Management

First, offer a calm, well-lit environment, careful explanations, consistent carers and ideally presence of a close relative, and explain and discuss with family/carers the treatment proposed.

Secondly

In absence of abnormal behaviour or perception or psychosis:

- Reduce anxiety if necessary with lorazepam 500microgram-1mg SL or PO or midazolam 2.5mg-5mg SC prn initially Benefit must be weighed against side effects such increased risk of falls.

In the presence of abnormal behaviour or perception or psychosis:

- to avoid excessive sedation, give haloperidol 500microgram-3mg SC or PO/24hrs (higher end of dose range only in severe distress; note subcutaneous:oral potency for haloperidol 2:1)
- Should sedation be required, use levomepromazine 12.5mg-50mg/24hrs in CSCI or PO.
- Acute confusion can be complex and difficult to manage so early involvement from the Palliative Care Team is recommended.

Hypercalcaemia of malignancy

Occurs in 10-20% of patients with malignant disease (especially breast cancer, squamous cell carcinoma, small cell carcinoma, renal cell carcinoma and myeloma); can occur in the absence of bone metastases.

Symptoms

- Confusion and drowsiness, anorexia, nausea and vomiting, constipation, polyuria and polydipsia
- Renal failure and coma may result if left untreated
- Symptoms may relate to the rate of rise in calcium but not necessarily to the degree of hypercalcaemia

Treatment is based on the corrected serum calcium mmol/l = {[40 – albumin g/l] x 0.02} + serum calcium mmol/l
The correction is important as this group of patients often have a low serum albumin.

Management

- Hypercalcaemia is often a poor prognostic sign and so it may not be appropriate to try to treat in the last few days of life.
- Correct dehydration.
- IV bisphosphonates (zoledronic acid, pamidronate or ibandronate) following hydration.
- Some drugs have a single specified dose. Others recommend a treatment dose dependent on initial albumin corrected plasma calcium concentration. In the latter case it has been suggested that the higher doses should be given irrespective of initial calcium level to increase likelihood of response and prolong duration
- Dose may need to be adjusted depending on renal function
- Effect seen within 3-7 days
- Repeat bloods should be arranged within 4 weeks as the treatment effect is usually temporary
- Drug and dose may need reviewing in refractory hypercalcaemia and advice sought from the Palliative Care Team.

Palliative management of breathlessness/dyspnoea

Breathlessness, the uncomfortable awareness of breathing, can be a frightening symptom and management of the fear and anxiety is an essential component.

Assessment

This includes history, examination and appropriate investigations. Reversible causes should be treated where possible. Symptomatic management requires a multidisciplinary approach and includes **both non-pharmacological** and pharmacological strategies. The relative contribution of these approaches will depend on the degree of breathlessness, patient's prognosis and the individual patient's preference. A model to help understand the components and how they interplay, Breathing, Thinking, Functioning (BTF) model has been proposed[7]. This model helps understanding and therefore targeting of interventions dependent on the variables driving the breathlessness.

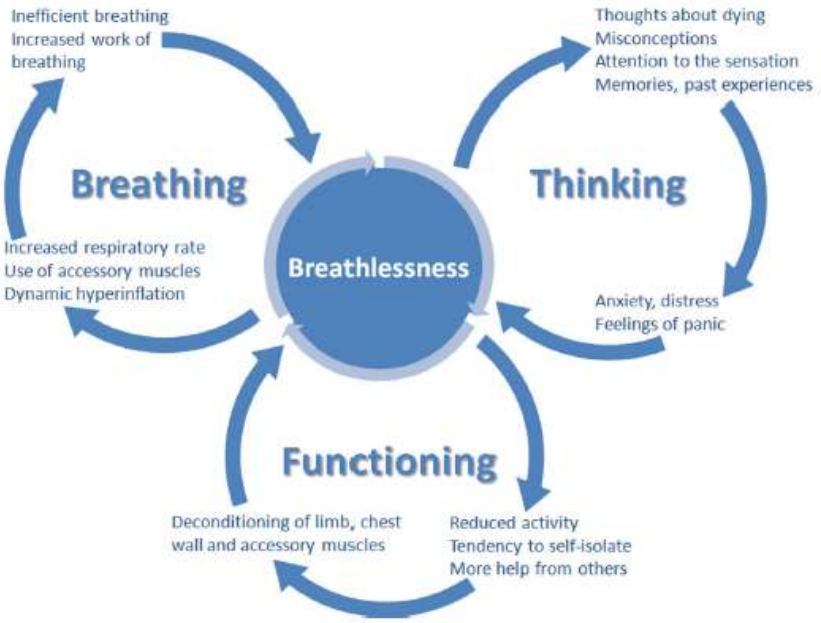


Fig. 1 The Breathing, Thinking, Functioning clinical model

Treat reversible causes where appropriate

E.g. pulmonary embolus; infection; reversible bronchoconstriction; pleural effusion; anaemia; cardiac failure; superior vena cava obstruction, (dexamethasone, radiotherapy or stent) or acute infective exacerbations of COPD.

Non-pharmacological strategies

- Should be employed in ALL patients who are breathless
- Exploration of fears, concerns and previous experiences
- Explanation and reassurance: e.g. "an awareness of breathlessness is normal after exercise and is not dangerous"
- Open, ventilated spaces and/or loosen tight clothes
- Simple advice: drop shoulders, breathe all the way out
- Hand held fan

- Calming support should be employed at all times:
    - “Position yourself where you feel fully supported and comfortable”
    - “When a muscle is tense relax it, by moving it in the opposite direction to the tension”
    - “Take a moment to feel that area become relaxed”
    - “Move each part of the body until the whole body feels relaxed”
    - “Think about a time or place where you felt relaxed”
    - “Take slow deep breaths and allow a quiet space for yourself”
- General adaptive measures include pacing, prioritising and planning activities e.g. move bed downstairs, sitting to wash, help with housework etc.
- Consider psychological therapies e.g. mindfulness based approaches, CBT
- Consider referral to a palliative care team and/or physiotherapist, e.g. refer to hospice breathlessness management service.

Pharmacological treatment

Opioids

- Reduce the sensation of breathlessness (supported by systematic review findings) with improvements seen at doses that do not cause respiratory depression.
- Modified release approach: start with MST Continus ® 5mg PO b.d. for 1 week. If baseline breathlessness not reduced ≥10%, increase by 10mg/24h weekly. Usual maximum 30mg/24h.
- In patients already taking regular opioids for pain then you may consider an increase in regular dose by 25-30%.
- The appropriate 4-hourly “as required” dose of morphine should be prescribed.
- Alternative opioids can be used for patients who cannot tolerate morphine.

Benzodiazepines

- Helpful in managing the fear and anxiety associated with breathlessness or acute episodes when this is a component driving the vicious cycle.
- E.g. lorazepam 500microgram-1mg prn/qdsuse with caution and limit maximum dose/24hr.

Nebulised 0.9% sodium chloride

- Helpful for sticky bronchial secretions that are difficult to expectorate

Carbocisteine – 375-750mg TDS may be useful in patients experiencing difficulty in expectoration.

Oxygen

- Useful in some patients, but there is no correlation with the degree of breathlessness and has no role if oxygen saturation is normal; seek specialist advice if in doubt.

Parenteral medication

If the patient is unable to take oral medication, and particularly in the last days of life, then morphine or equivalents at the appropriate conversion dose and midazolam can be given by CSCI and prn.

The dying patient

Recognising the dying patient

- The multi-professional team may agree that the patient is dying based on their clinical judgement of the underlying condition and progression.
- The following criteria may also apply:
  - Patient is bedbound
  - Patient is semi-conscious
  - Patient is no longer able to take tablets
  - Patient is only able to take sips of fluid

Checklist for the dying patient

- Ensure **reversible causes** for deterioration have been excluded or refused by the patient, or that potential interventions are agreed to be more burdensome than beneficial

- **Gather information** about the patient's physiological, psychological, social & spiritual needs, current symptoms, goals and wishes and views of those close to them, including Advance Decision to Refuse Treatment, Lasting Power of Attorney.

- **Communicate** to everyone involved to confirm the current situation.

- Clarify patient/family expectations, as well as that of the professionals involved and agree an **individualised plan of care**.

- Explain the **ceiling of treatment** rationale and clearly document.

- **DNACPR** form should be completed and explained.

- A treatment escalation plan/RESPECT form should be considered

- Confirm **Preferred Place of Death**- may lead to discharge home to die or hospice transfer.

- **Stop unnecessary medications**, observations and investigations.

- Ensure that **mouth care, bowel and bladder care** regimens are in place.

- Prescribe **anticipatory medications** for common symptoms in the dying phase.
  Appropriate prn SC medications are:

  - **Analgesia**: e.g. morphine 2.5mg-5mg SC 2-hourly if on no regular analgesia, or at the appropriate dose if already on opioids.
  - **Anti-emetic**: e.g. haloperidol 500microgram-1.5mg SC qds or cyclizine 50mg SC tds or levomepromazine 2.5mg-6.25mg SC qds
  - **Sedative**: midazolam 2.5-5mg SC 2-hourly
  - **Antimuscarinic** for respiratory secretions: glycopyrronium 200microgram SC 2-hourly or hyoscine butylbromide 20mg SC 2-hourly

- **Water for injection** to make up a syringe driver if needed.

- Review regularly to ensure the **symptoms are controlled**

- Consider **commencing a CSCI** if more than two doses of any of these medications are required.

- CSCI prescriptions should include an **appropriate range where possible** to prevent delays in symptom control. In the community doses can be started from zero if they are not needed at that time but might be in the future.

- Consider the place of **clinically assisted hydration and nutrition** and communicate the decision and rationale to the patient/carer(s) and document clearly.

- Consider **referral to the Palliative Care Team** either in the hospital or community.

- **Review regularly,** listen to everyone involved and communicate clearly changes or considerations in whatever setting you work (including your colleagues in and out of hours).

Respiratory secretions at the end of life

It is important to distinguish terminal respiratory tract secretions from conditions which may require alternative treatments e.g. left ventricular failure or pneumonia.

'Death rattle' is the noisy respiration caused by turbulent air passing through or over accumulated secretions in the oropharynx or bronchial tree in a patient who is close to death and unable to clear secretions by coughing and/or swallowing.

<u>General interventions</u>

- Repositioning of the patient (e.g. supine to lateral)
- Avoiding over-hydration
- Acknowledging and managing family distress with the audible noise

<u>Drug treatment</u>

- Glycopyrronium:
  - No central side effects
  - Longer half-life than other antimuscarinics
  - Dose: 200microgram SC prn and 600microgram-1.8mg/24 hours by CSCI.

Other medications that can be used are

- Hyoscine butylbromide: 20mg SC prn and 20mg-240mg/24 hours by CSCI.
- Hyoscine hydrobromide: 400microgram SC prn and 1.2mg-2.4mg/24 hours by CSCI.
  N.B. Can cause sedation or agitation.

<u>Other Measures</u>

- Manage associated breathlessness as per section above, p19.
- Antibiotics (when infected secretions are evident and distressing)

- Diuretics (when there is evidence of left ventricular failure)
- Agents to reduce the agitation if the secretions are contributing e.g. midazolam.

Suctioning usually only has a role in severe cases but is worth considering if symptoms are difficult to control.

Restlessness at the end of life

Patients may become restless in the last few days or hours of life.

Causes

May be physical, metabolic or psychological and precise aetiology may be difficult to identify and/or investigation of the cause may be inappropriate given the patient's poor prognosis.
It is, however, important to exclude easily treatable causes such as:

- Acute urinary retention
- Constipation
- Pain
- Drug toxicity
- Delirium with a clear reversible cause amenable to suitable treatment

Drug management of restlessness at the end of life

Aim to distinguish between anxiety and delirium to provide the most suitable management. The aim of treatment, which should be explained to family/friends, is to achieve relief of symptoms without preventing the patient from being able to communicate, using proportionate sedation. On some occasions symptom relief can only be achieved with sedation. If response is unsatisfactory, it is essential to review possible causes or contributing factors and seek palliative care team advice.

Midazolam

- 2.5mg-10mg SC stat and prn 4-hourly
- Consider midazolam 10mg-60mg/24 hours by CSCI. This can be gradually increased according to response. Larger doses may be used on specialist advice.

Levomepromazine

- Often useful in situations which fail to respond adequately to midazolam and in addition to it, particularly when delirium is a feature.
- 12.5mg–25mg SC prn 4-hourly
- 25mg-100mg/24 hours CSCI if on-going sedation required. Larger doses may be used on specialist advice

When symptoms are uncontrolled or severe, then prn medications maybe prescribed hourly until symptom control is achieved.

Symptom management in end stage heart failure

The general guidance in this document is pertinent to patients with end stage heart failure however the following cautions may need to be considered, depending on the patient's circumstances.

Pain

- Be aware that NSAIDS and COX-2 inhibitors may worsen heart failure and have been linked to increased risk of cardiovascular events.
- Patients with heart failure may also have renal impairment and in such cases appropriate guidance for opioid prescribing in renal impairment should be sought.
- Neuropathic agents can cause arrhythmias (tricyclic antidepressants) or fluid retention (pregabalin and gabapentin).

Nausea and vomiting

- Consider toxicity from medication especially digoxin.
- Commonly used anti-emetics in palliative care may have potential for undesirable cardiac side effects. However, any risks need to be balanced against good symptom control at end of life.
- Cyclizine may worsen severe heart failure and is generally avoided.
- Haloperidol, levomepromazine, domperidone, ondansetron can affect Q-T interval. Metoclopramide , rarely, can cause arrythmia in those at risk and mainly with IV use.
- If hypotension is a concern haloperidol and levomepromazine may exacerbate this. Use the lowest dose possible.

Breathlessness

- Ensure heart failure therapy is optimised including appropriate use of diuretics.
- Review doses and route of cardiac medication.
- If breathlessness persists see guidelines on page 17.

Cough

- Can be due to heart failure, drugs or other co-morbidity.

Constipation

- Avoid ispaghula husk because of fluid requirements.
- If using macrogols, lower sodium content is preferred.

Miscellaneous

- When using antidepressants – avoid tricyclic antidepressants and venlafaxine when possible.
- Steroids cause fluid retention.
- Consider oedema of the gastrointestinal tract as a possible cause of reduced efficacy of oral medications.

Withdrawal of medications and investigations

Symptom control should continue along with active cardiological management as long as this remains appropriate. As the patient's condition deteriorates and their prognosis reduces all drug therapy needs to be reviewed, along with the need for routine tests. In general, continue medications with short term symptomatic benefits and stop those aimed at medium to long term reductions in morbidity or mortality. If a patient is known to the heart failure team include them in this discussion.

Drug rationalisation needs to be individualised but the following guidance may be useful.

Medications which can probably be stopped or reduced as they are primarily for long term benefit:

- Lipid lowering agents
- Relax diabetic regimen
- Digoxin if in sinus rhythm

Medications which should be reviewed for risk versus benefit in the shorter term. This will vary depending on the individual:

- Anti-platelet medication
- Anti-coagulants
- Antihypertensives (monitor BP initially)
- Anti-anginals if no symptoms (monitor for symptom recurrence)
- ACE inhibitors
- Beta blockers

Medications which are likely to provide short term symptomatic benefit:

- Diuretics (unless too dry). Note furosemide can be given subcutaneously via syringe driver for symptom control. Seek advice from the Palliative Care Team.
- Anti-anginal medication if symptomatic.
- Rate control medication.

Implantable cardioverter-defibrillator should be de-activated according to local policy. If this has not been done or cannot than use of a permanently placed magnet is an option to deactivate the defibrillating capacity whilst applied over the ICD.

Symptom management in end stage renal disease

Drug doses often require modification in end stage renal disease (ESRD). Guidance is based on renal function but should be regarded as approximate and monitored for response**.**
For patients on dialysis, seek specialist advice**.**

Pain

Pain control in this group of patients is complex and requires early discussion with the palliative care and renal teams.
Some opioids and their active metabolites are renally excreted and will accumulate in renal impairment. Monitor patients for signs of opioid toxicity.

Appropriate adjuvants may be used at any step of the analgesic ladder

- Step 1- Paracetamol can be used safely unless severe renal impairment (eGFR <10) when dose reduction is required e.g. 500mg 6-8 hourly, maximum 3g/24hours.
- Step 2 - Tramadol is often used in reduced dose (e.g. 50mg12-hourly initially).
- Step 3 - General advice with opioids is to reduce dose and increase the interval between doses. Recommendations have been made for those with an eGFR below 30; at this level of impairment **regular** codeine, morphine, diamorphine and oxycodone **should be avoided**. As a prn oral opioid, immediate release oxycodone may be preferable to morphine.

Buprenorphine, fentanyl and alfentanil are the opioids least likely to accumulate. Refer to Opioid Conversion Table or access the online “Pallicalc” at http://book.pallcare.info/index.php for equivalent doses.

An NSAID may be used in normal doses if pain control is a clear priority over maintaining existing renal function.

Pregabalin and gabapentin require dose adjustment in renal impairment (see BNF).

Amitriptyline can be used with a low starting dose e.g. 10mg nocte.

Nausea and vomiting

Anti-emetics can accumulate in renal impairment. There may be increased cerebral sensitivity to drugs such as haloperidol and levomepromazine and increased risk of extrapyramidal side effects with metoclopramide. The choice of anti-emetic will depend on the cause of nausea and vomiting. Monitor for side effects.
Examples of anti-emetics and suggested initial doses:

- cyclizine, ondansetron, granisetron: dose as in normal renal function
- domperidone: 10mg od–bd
- metoclopramide: 5mg tds-10mg tds
- haloperidol: with occasional use dose may be unchanged however if more regular use 500 microgram-1mg PO/SC prn 8-hourly or 1.5mg-3mg via CSCI over 24hrs
- levomepromazine: lower doses may be sufficient e.g. 2.5mg-6.25mg SC nocte or prn 8-hourly, or via CSCI starting at 6.25mg/24 hours.

Dyspnoea/breathlessness

General management is the same.
Opioids may be trialled for refractory symptoms though evidence is lacking for those opioids considered safer in renal failure.
Benzodiazepines accumulate in renal impairment but can be used in lower doses for anxiety associated with breathlessness.

Respiratory tract secretions

There is no difference in the management in renal failure.

Delirium (or agitation) at the end of life

Midazolam 2.5mg SC prn or by CSCI starting at 5mg-10mg/24hours; this can be gradually titrated up.
Haloperidol 0.5 - 1mg SC prn or by CSCI starting at 1.5 -3mg/24 hrs with titration as required.

Levomepromazine 2.5 - 6.25mg SC prn or by CSCI starting at 6.25mg/24 hours with titration as required

Delirium at the end of life

Benzodiazepines accumulate in renal impairment so the starting doses are lower e.g. midazolam 2.5mg SC prn or by CSCI, 5mg-10mg/24hours; this can be gradually titrated up according to severity of anxiety or agitation.
Haloperidol or levomepromazine can also be used if required.

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Pruritis

This can be challenging to manage.
Topical emollients are first line treatment.
If localised capsaicin cream 0.025 - 0.075% od - qds may be considered
Cetirizine 5mg or 10mg od or chlorphenamine 4mg tds/qds can be tried
Low dose gabapentin e.g.100mg daily or after dialysis, or pregabalin 25mg daily or after dialysis may be useful.
Discuss with Palliative Care Team regarding other options if these measures are not successful.

Restless leg syndrome

Seek advice from palliative care team.

Diabetes Mellitus in patients approaching the end of life

Fine control of a patient's blood sugars should be replaced with prevention of short-term complications and the control of symptoms.
Aim for a blood glucose in the range of 6-15mmol/l.[8]
This should avoid hypoglycaemia and symptomatic hyperglycaemia preventing acute complications of diabetic ketoacidosis or the hyperosmolar non-ketotic state.

Factors that might affect diabetic control at the end of life:

- Appetite and calorie intake
- Symptoms such as nausea and vomiting
- Cachexia
- Medication including the use of steroids at the end of life
- Concurrent infection
- Liver metastatic involvement - impaired gluconeogenesis
- Impaired drug clearance of diabetic medications e.g. sulphonylureas

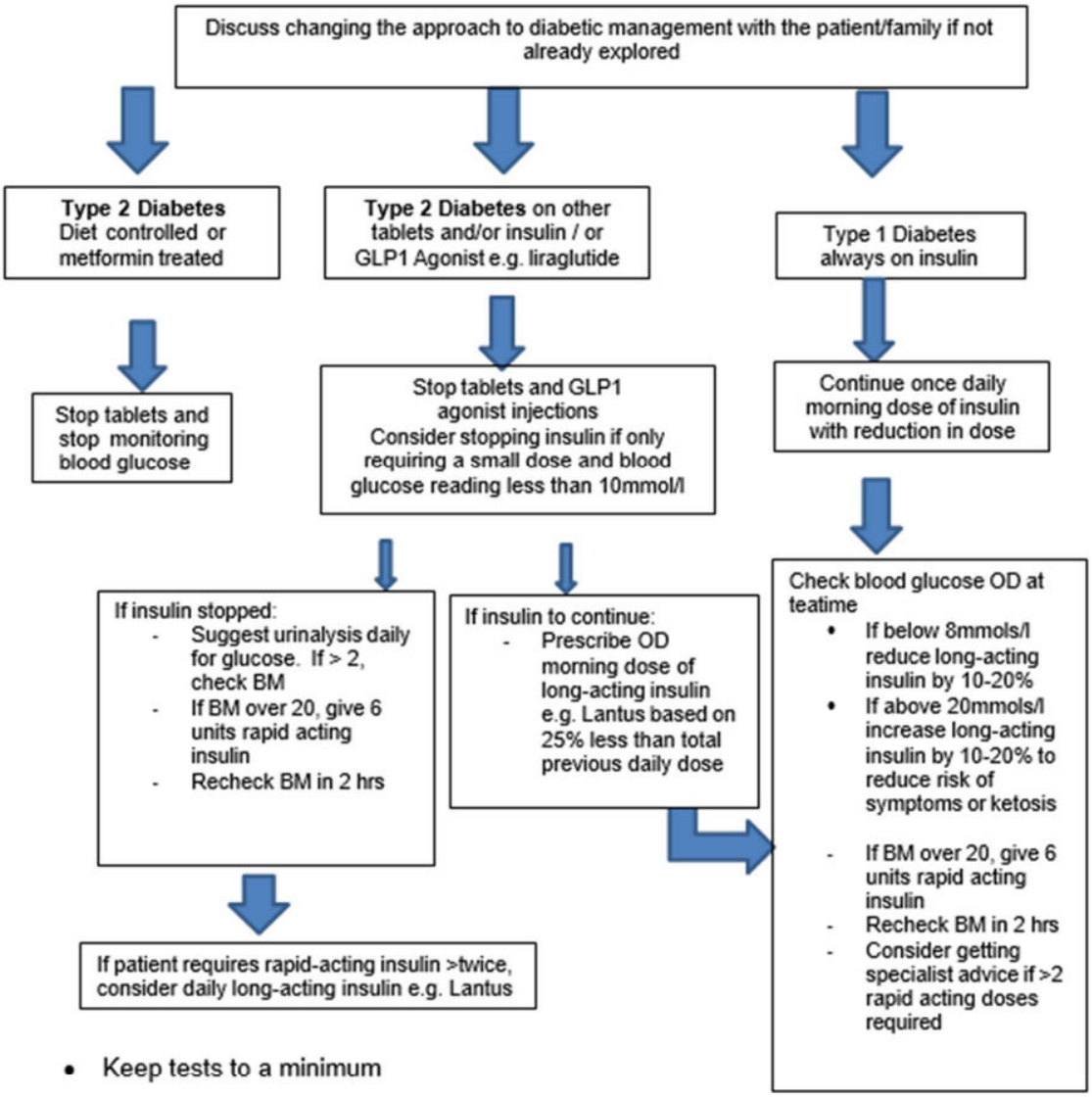
The management plan for the control of blood sugars in patients approaching the end of life with diabetes will vary dependent on:

- Prognosis
- Presence of symptoms requiring careful assessment for hypo or hyperglycaemia
- Aetiology of the diabetes. Whether type 1 or type 2

General management

- Dietary advice - adjusting medication is preferable to limiting the patients diet, but therapy should match small frequent meals.
- Reassess medication in particular the corticosteroid dose and reduce if possible.
- Look at de-intensifying other therapies in discussion with patient and families/ carers.
- Insulin dose requirements reduce towards end of life as appetite reduces, weight falls and activity reduces.
- Do not stop insulin in those with type 1 diabetes.
- Early discussion with patient and family, possibly also involving input from the diabetes nurse specialists, in order to agree on a management plan is advisable.
- Keep blood glucose monitoring to a minimum. A urine dipstick for glucose might be sufficient with a positive result prompting blood sugar measurement. Stopping monitoring altogether in the terminal phase should be considered.
- Involve the diabetic specialist Pump team in Type 1 diabetics who have insulin pump treatment.

Algorithm for the last days of life – adapted from Diabetes UK End of Life Care November 2021 Guidelines



- Keep tests to a minimum
- It is difficult to discern between symptoms of hypo and hyperglycaemia in a dying patient
- Test urine or blood for glucose if the patient is symptomatic
- Observe for symptoms in previously insulin-treated patients, if insulin is discontinued
- Flash glucose monitoring may be useful to avoid finger prick testing

Sick-day management [8]

Sick day rules are used in patients who may be unwell due to inter-current illness or side effects from treatment. It is important to review ceilings of treatment with patients i.e. for hospital transfer or not.

Type 2 Diabetes	
Type 2 managed by diet alone or tablets that are NOT sulphonylureas e.g. gliclazide, or prandial regulators (glinides)	**Type 2 managed by sulphonylureas, prandial regulators and/or insulin or GLP1 agonist**
Continue usual diabetic medication but STOP SGLTs agents e.g. dapaglifozin and metformin in acute illness	Check blood glucose only to confirm symptoms of hypo or hyperglycaemia
Offer frequent small portions of easily-digested foods or fluids Sip sugar-free fluids regularly (aim for 100ml/hr)	Offer frequent small easily digested carbohydrate foods if unable to eat normally. Offer sips of sugar-free fluid aiming for 100ml/hr
Observe for signs of hyperglycaemia and dehydration Check capillary blood glucose to confirm hyperglycaemia	If blood glucose >15mmol/l consider increasing the sulphonylurea or insulin dose If blood glucose less than 6mmol/l then consider reducing the insulin or sulphonylurea dose
Aim to maintain blood glucose 15mmol/l or less If blood glucose >15mmol/l then consider giving short acting insulin	Glycaemic treatments may be discontinued if the patient is not eating, and blood glucose <15mmol/l and the patient is asymptomatic

Type 1 Diabetes
DO NOT DISCONTINUE INSULIN TREATMENT
Sip sugar free fluids regularly (aim for 100ml/hr)
If unable to eat normally, offer frequent small portions of easily digested foods or fluids
Test for urine or blood ketones if patient shows signs or symptoms of hyperglycaemia and dehydration. If positive, test blood glucose and ketones every 2hrs. Continue usual daily insulin, consider giving short-acting insulin (10% of usual daily insulin dose) every 2 hours until ketones no longer present. Consider getting specialist advice and reviewing ceilings of care with the patient if this has not been done already.

Hospital admission may be appropriate for IV rehydration and insulin therapy.

Management of hypoglycaemia [8]

Identifying those at risk:

These include patients being administered insulin, sulphonylurea (e.g. Gliclazide, Glipizide, Glimepiride), prandial regulator users (Nateglinide, Repaglinide) and SGLT-2 inhibitors (e.g. dapagliflozin, gliflozin, etc…)
Patients who are at particular high risk include those who also have one or more of the following:

- Poor appetite/erratic eating pattern
- Weight loss
- Renal deterioration
- Liver impairment/ carcinoma
- Nausea and vomiting
- Autonomic neuropathy
- Oropharyngeal and oesophageal cancers
- Previous gastrectomy
- Frailty
- Memory problems

- Hypoglycaemia is a significant risk as anorexia develops.
- Glucagon may not be effective especially in those malnourished, the presence of liver disease and those with repeated hypoglycaemia.
- The oral or buccal route is preferable in terms of immediate management but the integrity of the patient's swallow, and therefore the safety of use of this route, needs to be rapidly assessed.

Conscious level and swallow	Management
Able to swallow safely	Consider fruit juice e.g. 200ml pure smooth orange juice, sugary fizzy drinks, 60mls Fortijuice/Ensure plus, glucose/dextrose tablets, or 40% Glucose gels, up to x2 tubes slowly inserted into buccal cavity.

Conscious and not able to swallow	PEG tubes can be used as a route of administration for glucojuice/ fortijuice/ ensure juice
Unconscious	Place the patient in the recovery position as this is the priority if unconscious. 1mg Glucagon can be given intramuscularly if available. If unavailable or ineffective then intravenous access and a 50-100ml bolus of 20% Dextrose given over 10-15mins if appropriate. Consider transfer to the acute sector if in line with the patient's ceiling of appropriate management.

- Repeat observation regularly and blood sugar monitoring every 10-15minutes until blood sugar is stable at over 4 mmol/l.
- Give foods rich in starchy carbohydrate e.g. banana, x2 plain biscuits or glass of milk, that release their energy slowly to reduce the risk of recurrence.
- Continue to monitor as there is increased risk of recurrent hypoglycaemia in those receiving glucagon.
- Review insulin or oral hypoglycaemic agents to minimize risk of recurrence.

Symptom management in end stage Parkinsonism

Usual Treatment

The NICE clinical guideline on Parkinson's disease emphasises that palliative care requirements should be considered throughout all phases of the disease.
If patients are unable to tolerate their standard treatment it should be substituted appropriately without delay with advice from the Parkinson's or movement disorder specialist team.
The key principles are that anti-Parkinson's medications:

- should not be withdrawn abruptly or allowed to fail suddenly due to poor absorption. This may result in acute akinesia or neuroleptic malignant syndrome;
- should be given at appropriate times;
- should be adjusted by, or adjusted only after discussion with, clinicians experienced in the management of Parkinson's disease.
- When the oral route for medicines administration is lost consider a Rotigotine patch. See www.parkinsonscalculator.com for dose calculations.

Drugs used for symptom relief

Standard symptom control regimens may need to be adjusted in patients with Parkinsonism. Neuroleptics and anti-emetics in particular may result in symptoms of muscle cramps, impaired swallowing, rigidity and fever. This may culminate in the neuroleptic malignant syndrome, a potentially life-threatening condition. In the last hours or days of life this may be less of a concern if effective symptom control outweighs the risk of side-effects.

Pain

Consider the potential for interaction with MAO-B inhibitors. Tramadol, pethidine, some other narcotics and SSRIs could give a serotonin-like syndrome. Muscle cramps and myoclonus are best treated by benzodiazepines like clonazepam.

Nausea and vomiting

Dopamine antagonists (e.g. haloperidol, prochlorperazine, metoclopramide) are likely to aggravate symptoms.
Domperidone 20mg PO tds or 30mg rectally is the first-line agent.
Ondansetron is an option (contraindicated with MAO-Bs).

Confusion and psychosis

This is common, and in true Parkinson's disease can be a marker of progression to end stage disease. At this point anti-Parkinson's medications may need to be reduced carefully to maintain quality of life. Acetylcholinesterase-inhibiting drugs are effective in these situations. They should not be stopped without good reason.
Treatment, where necessary, is with benzodiazepines or the atypical antipsychotic quetiapine starting at a low dose (e.g. 12.5mg). Avoid the usual antipsychotics (e.g. haloperidol).

Specialist Advice

Most advanced patients will already be known to local Parkinson's disease nurses or movement disorder services. Clinical staff relatively inexperienced in managing the end stages of Parkinsonism should consider seeking specialist advice.

Communication: Breaking bad news and CPR discussions

Communication at the end of life: Key points

- Advance care planning is important and requires competent communication skills and confidence
- Communication needs to be open between patients, families and all professionals involved
- Listen to and understand what the patient's issues are; active listening skills are essential
- The non-verbal message you give is as important as the verbal one (e.g. tone of voice, physical demeanor).

Breaking bad news

The following steps may help in structuring these conversations:

1. Preparation: setting the scene – ask who should be present; ensure you have up-to-date information

2. Gain the patient's/carer's perspective and their understanding of the information they have received already; how close are the patient's ideas to the actual situation? Use their words and phrases to help with explanations
3. Find out what the patient wants to know and tailor your information accordingly
4. When giving new information, give a warning shot and allow time for this information to be digested
5. Allow the patient to guide how much information they require at this time; you may need to stop the consultation and arrange a further appointment
6. Offer explanation if requested: honest and simple language, in small chunks, avoiding jargon and checking understanding; it is helpful to encourage questions.
7. Elicit concerns and encourage expression of feelings and emotions, this can be therapeutic in itself. Acknowledging the emotional impact (empathy) of the delivered information is important for the patient to appreciate the impact of delivered information. Correct immediate misunderstandings and identify appropriate longer-term support as negotiated with the patient/carer.
8. Summary and plan: Confirm understanding from all perspectives and agree a plan of action and review date for the future.
9. Offer realistic availability and support, early follow-up maybe required dependent on the individual's emotional state and levels of support.
10. Communicate with wider team.

Discussions about cardiopulmonary resuscitation (CPR)

Clear leadership, explanation and communication with patients and their families is vital to manage this challenging area of end-of-life care. Patients should be informed and involved. If the patient is not willing to be involved in discussions, or if there is a risk of significant psychological harm in proceeding with discussions with the patient, document this and the reasons carefully.

When the patient is at an advanced stage of dying from an irreversible condition, CPR is contraindicated. Likewise, when the patient has an advanced illness and deteriorating health such that CPR will not work, the discussion should focus on the care of the dying patient.

The family's role is to inform the process and be aware of why a decision is being made and not to make a final decision. When this is not understood relatives can feel they are carrying the burden of a decision.
Do not ask "shall we resuscitate your relative?" as CPR is a medical intervention that will only be offered if it is felt to have a reasonable chance of working.
It may be useful to adopt a similar approach to breaking bad news when having discussions relating to CPR

1. Preparation.
2. Seek permission to explore expectations of their illness and treatments;
   "We would like to talk about your future care and management, would that be OK?"
   "I would like to talk through some of the things that may happen to you and how we would we manage them? How do you feel about that?"
3. Assess current level of understanding about resuscitation and provide an appropriate warning shot;
   "Tell me what you understand about how your illness is progressing"
   "How do you see the future?"

4. Explain to patients and their families that attempts at CPR are very unlikely to be a successful for the significant majority of patients with advancing / progressive illness. Remember to chunk and check the volume of information as before;
   "We are concerned you may be dying now and that we need to focus on maintaining your comfort"
   Or:
   "Whilst we will try to get you as comfortable as we can, there are some procedures that will not help and will probably be more burdensome than beneficial; such as CPR / ventilation / clinically assisted nutrition and hydration."
5. Include other ceilings of treatment that are appropriate and future care wishes such as preferred place of care and death.
6. Explore feelings and offer opportunity for questions.
   "How does this leave you feeling? What questions would you like to ask?"
7. Arrange follow-up as appropriate, ensuring the DNACPR form is completed and there is documentation reflecting a summary of the discussions. The patient should keep the red, top copy with them whatever the setting of care.

This approach acts as a guide as to how a discussion may be led. The exact phrases used should be determined by the patient and their responses to previous questions and/ or information.

Use electronic Palliative Care coordination systems (EPaCCS), to communicate across specialties, disciplines and settings e.g RESPECT Where these are unavailable, ensure that DNACPR decisions are communicated with key members of the patient's healthcare team, e.g. GP via electronic discharge notifications or in clinic letters.

Regionally approved 'Do Not Attempt CPR' forms stay with the patient to ensure inappropriate attempts at CPR are not initiated.

This information is vital for all professionals involved in care including ambulance crew, community nurses, care homes and care agencies.

Where there is disagreement between patients, families and professionals, it may help to allow more time (if possible), to offer written information or a second opinion could be sought.

Your own needs

Communication skills training is essential for all those involved with communication near the end of life and delivering bad news.

Adult specialist palliative care units and teams in Kent

Ashford

Pilgrims Hospices in Ashford
☎01233 504133 (24 hour)
ph.pilgrimshospices@nhs.net

William Harvey Hospital Macmillan Palliative Care Team
☎01233 633331 via switchboard

Canterbury

Pilgrims Hospices in Canterbury
☎01233 504133 (24 hour)
ph.pilgrimshospices@nhs.net

Kent and Canterbury Hospital Palliative Care Team
☎01227 766877 via switchboard

Dartford, Gravesham and Swanley

ellenor Hospice (24hour)
☎01474 320007
telh.clinical-admin@nhs.net

Darent Valley Hospital Palliative Care Team
☎01322 428293
dgn-tr.palliativecare@nhs.net

Maidstone

The Heart of Kent Hospice
☎01622 792200
THO.ClinicalAdminHoKH@nhs.net

Maidstone Hospital Macmillan Palliative Care Team
☎01622 225024 (bleep 1425 or 1133)

Margate

Pilgrims Hospices in Thanet
☎01233 504133 (24 hour)
ph.pilgrimshospices@nhs.net

QEQM Hospital Palliative Care Team
☎01843 225544 via switchboard

Medway and Swale

Medway Community Healthcare CIC:
Wisdom Hospice,
☎01634 830456
wisdom.hospice@nhs.net

Medway Maritime Hospital, Hospital Palliative Care Team
☎01634 833807
MEDCH.HPCT@nhs.net

Tunbridge Wells

Hospice in the Weald
☎01892 820500
hitw.hospice@nhs.net

Tunbridge Wells Hospital Macmillan Palliative Care Team
☎01892 -635675 (bleep 2346 or 2397)

Further Reading and References

www.palliativedrugs.com

Palliative Care Formulary 7th Edition, available from palliativedrugs.com

More detailed palliative care guidance and access to "pallicalc" and "palliap":
http://book.pallcare.info/index.php

NHS Scotland Palliative Care Guidelines App

"Decisions relating to cardiopulmonary resuscitation", 3rd edition (1st revision) a 2016 joint statement from the British Medical Association, the Resuscitation Council (UK) and the Royal College of Nursing

General Medical Council 2010 *"Treatment and care towards the end of life: good practice in decision making"*

Macmillan leaflet *"Cardiopulmonary resuscitation (CPR) for people with cancer"* available on their website.

The renal drug handbook – 5th edition, editors Ashley C, Dunleavy A

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2. World Health Organisation (1996)
3. Ballantyne JC et al WHO analgesic ladder: a good concept gone astray. *BMJ 2016;352:i20*
4. Opioids for persistent pain: summary of guidance on good practice from the British Pain Society. *British Journal of Pain:*6(1) 9–10
5. Els C, Jackson TD, Hagtvedt R, Kunyk D, Sonnenberg B, Lappi VG, Straube S. High-dose opioids for chronic noncancer pain: an overview of Cochrane Reviews. *Cochrane Database of Systematic Reviews* 2017, Issue 10. Art. No.: D012299. DOI:10.1002/14651858.CD012299.pub2.
6. Chou R et al. The Effectiveness and Risks of Long-Term Opioid Therapy for Chronic Pain: A Systematic Review for a National Institute of Health Pathways to Prevention Workshop. *Ann Intern Med.* 2015;162:276-286. doi:10.7326/M14-2559
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8. Diabetes UK. End of Life Care. March 2018. https://www.diabetes.org.uk/Professionals/Position-statements-reports/Diagnosis-ongoing-management-monitoring/End-of-Life-Care. Accessed August 2018.

Guidelines for the use of naloxone in iatrogenic opioid overdose in palliative care

DO NOT USE WITH BUPRENORPHINE

For a patient with EIGHT or more respirations per minute, who is easily rousable and is not cyanosed, wait and see; next oral opioid dose either reduced or omitted.
If a continuous infusion is in place (*e.g.* a syringe driver) then the appropriateness of the dosage delivered must be reviewed; the driver can be stopped for a period and/or dose reduced.

If the respiratory rate is less than EIGHT breaths per minute (or is higher than this but dropping rapidly), and the patient is barely rousable, unconscious or cyanosed then the following action should be taken:

NOTE: Naloxone is best given intravenously (onset of action 1-2 minutes), but if not practical (*e.g.* IV access is difficult or IV trained staff are not available) then it may be given intramuscularly or subcutaneously (onset of action 2-5 minutes).

1. Discontinue any further administration of strong opioids.
2. Dilute 400micrograms of naloxone to 4mls with 0.9% sodium chloride to get 100mcg/ml
3. If intravenous access is available go to step 4; otherwise administer 40 micrograms intramuscularly.
4. Administer 1ml (one hundred micrograms) intravenously (**see notes in bold above**) every two minutes until the respiratory rate is satisfactory. In some case lower doses, 20mcg, can be used safely.
5. This guidance is different from the management of an immediately life threateiening respiratory depression where a standard starting dose of naloxone 400mcg is recommended, in the context where the patient is already NOT on long term opiates.

Titrate dose against respiratory function, not level of consciousness
Total antagonism will cause a return of severe pain with hyperalgesia, potentially severe physical withdrawal symptoms and marked agitation.

Opioid antagonism caused by naloxone lasts for 15 to 90 minutes. As most immediate release opioids have an action of 4 hours and sustained release preparations either 12 or 24 hours, it is important to continue to closely monitor the patient as further absorption of the opioid will result in recurrent respiratory depression necessitating further doses of naloxone

Before any strong opioids are recommenced, the prescriber must review the patient's requirements and decide an appropriate course of action.

Syringe driver compatibilities

	Cyclizine	Glycopyrronium	Haloperidol	Hyoscine Butylbromide	Hyoscine Hydrobromide	Levomepromazine	Metoclopramide	midazolam	Morphine	Oxycodone
Cyclizine		✓	✓	⊘	✓	✓	⊘		✓	✓
Glycopyrronium	✓		✓	No data	No data	✓	✓	✓	✓	✓
Haloperidol	✓	✓		✓	✓	✓	✓	✓	✓	✓
Hyoscine Butylbromide	⊘	No data	✓		✓	✓	✓	✓	✓	✓
Hyoscine Hydrobromide	✓	No data	✓	✓		✓	✓	✓	✓	✓
Levomepromazine	✓	✓	✓	✓	✓		✓	✓	✓	✓
Metoclopramide	⊘	✓	✓	✓	✓	✓		✓	✓	
Midazolam	✓	✓	✓	✓	✓	✓	✓		✓	✓
Morphine	✓	✓	✓	✓	✓	✓	✓	✓		NA
Oxycodone	✓	✓	✓	✓	✓	✓	✓	✓	NA	

Key

✓	= Compatible at usual concentrations
⊘	= not suitable to be used together
✓	= dilute in sterile water no greater than 10mg/ml

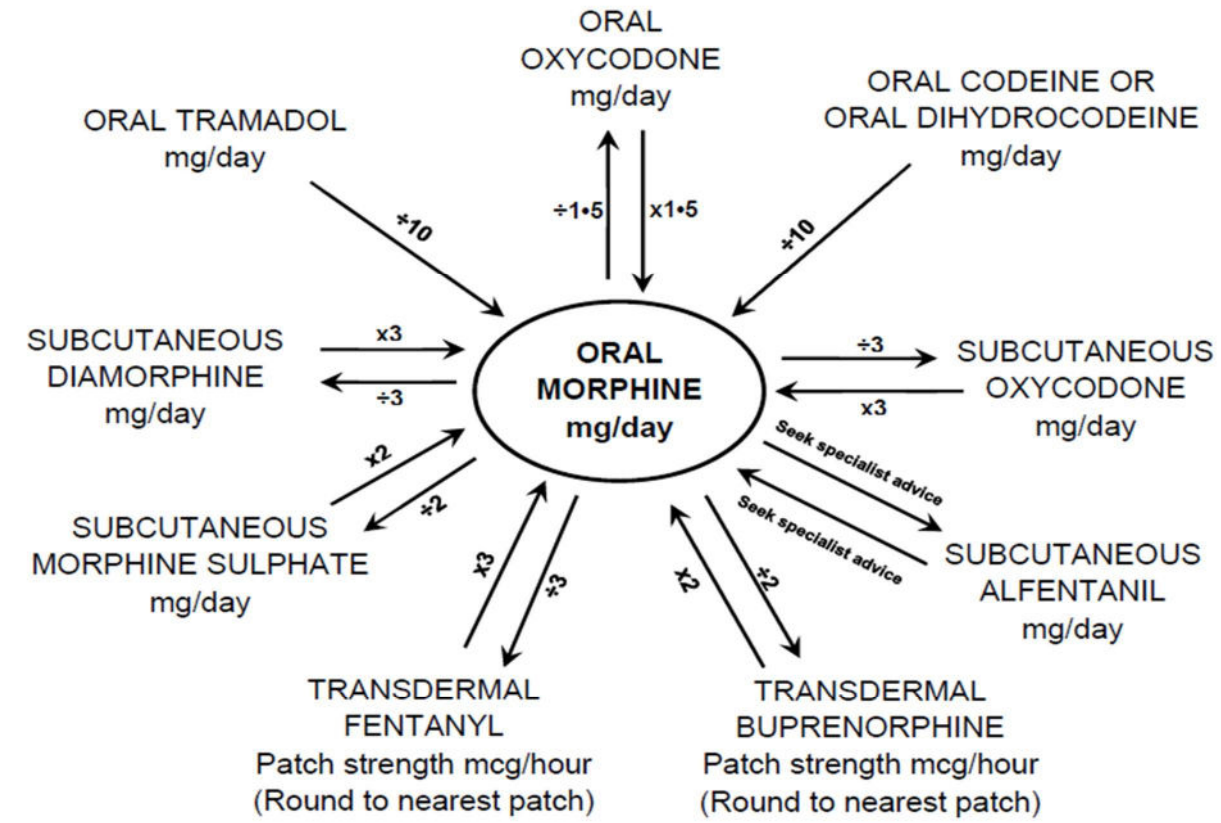
More detailed compatibility information is now available on the medicines complete website medicinescomplete.com

Opioid conversions

Please note that the equivalence doses of opioids are never more than an approximate guide. Thus, careful monitoring during conversion is necessary to avoid both under-dosing and excessive dosing.

Two different approaches to calculating equivalent doses have been provided as some colleagues may find one or the other method more helpful. The two methods may not result in exactly the same dosage conversion, but note that this is not an exact science and that individual patient factors and responses need to be taken into account.

The Leeds Opioid Conversion Guide For Adult Palliative Care Patients



Always go through the centre of the chart (via oral morphine) when converting between opioids.

St. Gemma's Hospice

Leeds Community Healthcare NHS Trust

The Leeds Teaching Hospitals NHS

Sue Ryder Wheatfields Hospice

NOTES : This chart is intended for guidance, prescribers are responsible for their own decisions.

All calculations and rationale must be documented in the patient's record, including those for prn doses.

Clinical judgement should be applied, considering: underlying clinical situation; comorbidity (e.g. renal or liver impairment); drug interactions, nature of pain and its opioid responsiveness; other pain interventions; symptoms being managed by opioid; toxicity of current opioid; previous opioid doses and adherence; rapidity of opioid escalation; use of larger doses; switches involving change of route; malabsorption issues; reason for switching. These factors **may** necessitate an empirical reduction in the dose of the replacement opioid and re-titration.

For further advice contact your local Specialist Palliative Care Service.

Conversions are based on Company Data, PCF5 and EAPC 2011 guidelines.

Adapted for Leeds city wide use April 2016 (Leeds Palliative Care MCN)

Assessed Online – 11th March 2019

West Kent Guide to Equivalent Doses for Opioids (July 2016)

The preferred option for the calculation of opioid conversions is to use the on-line converter or associated "app":
Kent and Medway Palliative Care Guidelines, http://book.pallcare.info/index.php?op=plugin&src=opiconv

This chart provides approximate equivalent doses for opioids and only forms part of a prescribing decision. Advice should be sought from the palliative care team if there are uncertainties about how to prescribe for individual patients (e.g. when higher doses are required, renal impairment, concerns about lack of response when titrating medications).

Morphine					Oxycodone				Diamorphine		Alfentanil		
Oral			Parenteral		Oral		Parenteral		Parenteral		Parenteral	Transdermal	
24 Hour total morphine		Morphine modified release tabs	Morphine oral solution or tabs	Morphine by CSCI	Morphine prn SC	Oxycontin modified release tabs	Oxynorm oral	Oxynorm by CSCI	Oxynorm prn SC	Diamorphine by CSCI	Diamorphine prn	Alfentanil by CSCI	Fentanyl DTrans matrix Patch	Buprenorphine patch
mg/24 hrs		mg/12 hrs	mg/4 hrs	mg/24 hrs	mg/prn	mg/12 hrs	mg/4 hrs	mg/24 hrs	mg/prn	mg/24 hrs	mg / prn	mg/24hours	micrograms/hr	micrograms/hr
30		15	5	15	2.5	10	2.5	10	2.5	10	2.5	1	12	10
60		30	10	30	5	15	5	15	2.5	20	5	2	25	20
100		50	15	50	7.5	25	10	25	5	30	5	3	37	35
120		60	20	60	10	30	10	30	5	40	7.5	4	50	52.5
180		90	30	90	15	45	15	45	7.5	60	10	6	75	70
240		120	40	120	20	60	20	60	10	80	15	8	100	105
360		180	60	180	30	90	30	90	15	120	20	12	150	140
480		240	80	240	40	120	40	120	20	160	25	16	200	
600		300	100	300	50	150	50	150	30	200	35	20	250	
800		400	130	400		200	70	200	35	250	40	25	325	
1000		500	160			250	80	250	40	300	50	30	400	
1200		600	200			300	100	300	50	400	60	40	500	

- The conversions given in this table are a pragmatic mix of "traditional" and "progressive" methods use in the on-line converter tool. Dose conversions should be individualised and will require adjustment according to response. Consider a dose reduction of 25-50% to allow for incomplete cross-tolerance.
- Higher doses of morphine are too large a volume for SC injection.

- Oxynorm injections beyond 20mg as a prn dose and 200mg via syringe driver will require the Oxynorm concentrated injection of 50mg/ml which is expensive.
- Use caution when calculating opioid equivalence for transdermal patches. Conversions to and from fentanyl and buprenorphine patches should be checked against the manufacturer's guidance.
- For other opioids, e.g. codeine, tramadol, please refer to on-line converter.