Symptom Control and Care of the Dying Patient: Palliative Care Guidelines

5th Edition

Produced by Kent Palliative Medicine Forum

Whilst every effort is made to ensure the accuracy of this guide, the authors and organisations supporting it cannot accept any liability for any inaccuracies.

Some recommendations are based on accepted practice, using medications outside of their product licence and not always with good research evidence to support this.

Please refer to the PCF5 as a more definitive guide if in any doubt.

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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.
Note: 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, especially the palliative care section.

Doses

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

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Abbreviations

SL	Sublingual
SC	Subcutaneous
IM	Intramuscular
PO	Per oral
IV	Intravenous
CSCI	Continuous subcutaneous infusion via a syringe driver
od	Once daily
bd	Twice daily
tds	Three times a day
qds	Four times a day
prn	As required
hr	hour
mg	milligrams
g	grams
mmol/l	millimols per litre
NSAID	Non-steroidal anti-inflammatory drug

The management of pain

A holistic approach is necessary when dealing with pain control in terminal illness. There may be several factors contributing to the experience of pain such as:

Psychological fears

The fears and concerns of the patient.

Social concerns

Patients are part of a wider social network and may have concerns regarding them.

Spiritual distress

The meaning of the illness to the patient which may lead to questions about the meaning of life - "why me?" "what next?".

Principles of good pain control
• Assess the patient and explore their concerns and expectations. • Help patients and their carers to understand symptoms • Treat the cause of the pain where possible • Use the analgesic ladder at the appropriate step • Prescribe analgesia on a regular basis • Prescribe appropriate analgesic for breakthrough pain • Explain the management plan to patient and carer • Review analgesic needs frequently

Assessment

- What is the cause of the pain?
  - Treat reversible causes.
  - Carefully exclude conditions requiring intervention such as spinal cord compression, fracture and infection.
- What are the characteristics and severity of the pain?
  - Assess by the impact on activities of daily living or interference with rest / sleep.
- What is the **type** of pain: neuropathic, bone, visceral, etc?

- What associated social, psychological, spiritual and physical issues are present?

Management

- All patients require a full explanation of what is happening
- Most patients require regular analgesia, and may also require specific treatments aimed at underlying causes (*e.g.* palliative radiotherapy for metastatic bone pain)
- Start at an appropriate step of the ladder. If you are aware or suspect patient has renal impairment please see section on renal failure regarding analgesia use (Page 23)

STEP 3	Strong opioids *e.g.* morphine +/- non opioid +/- adjuvant analgesia
STEP 2	Weak opioids *e.g.* codeine +/- non opioid +/- adjuvant analgesia
STEP 1	Non opioid *e.g.* paracetamol +/-adjuvant analgesics

The usual starting doses on each step are:

- Step 1: Paracetamol 1g po qds
- Step 2: Codeine 30-60mg po qds (note steps 1 and 2 may be combined as co-codamol 30/500 two tablets qds)
- Step 3: Immediate Release morphine 5-10mg every 4 hours OR slow release morphine (*e.g.* Zomorph capsules or MST tablets) 10mg-30mg every 12 hours.
  Refer to the conversion chart or access the online resource "Pallicalc" at http://book.pallcare.info/index.php for an appropriate starting dose of morphine if previously on maximum dose of a step 2 opioid.

For patients commencing morphine, an as required ("breakthrough") dose should also be prescribed:

- Immediate release morphine (*e.g.* Oramorph liquid or Sevredol tablets) should be prescribed PRN 4 hourly at a dose of 1/6th of the 24hour oral morphine dose *e.g.* a patient taking 90mg BD of slow release morphine is the equivalent of 180mg in 24 hours and so would receive 30mg of immediate release morphine as breakthrough.
- Increased use of breakthrough analgesia, for example more than 3 doses in 24 hours requires review of the regular dose and this may need increasing.

If pain is severe then it is good practice to start at step 3 *i.e.* strong opioids. Continue to titrate up the morphine dose by up to 30% every 24-48 hours until pain relief is satisfactory or side-effects occur.

If patients are unable to take oral analgesia, then opioid analgesia should usually be given SC. The 24 hour dose is given via a syringe driver (CSCI) as a continuous infusion.

Alternative opioids

Other opioid drugs are available and are sometimes used for palliative care patients. Morphine remains the first choice, although there may be specific indications where alternatives are indicated such as renal failure or intolerable side effects. The opioid conversion chart or the online "Pallicalc" at http://book.pallcare.info/index.php gives the relative potency of these medications helping to guide conversions from one opioid to another.

Oxycodone(PO/SC)

Oxycodone provides an alternative to opioid to morphine. It has a role if patients develop intolerable side-effects from morphine.

Alfentanil Injection

This may be of use in patients with significant renal impairment. Please contact the Palliative Care Team for further advice.

Transdermal Opioids (Patches)

These should only be used for patients who have 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 side-effects to other opioids
- 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 that the brand name is used.

Ensure the patient and carers are counselled about correct usage and disposal of patches (seek advice from the Palliative Care Team if needed)

Fentanyl Patches

Patch strengths: 12 micrograms/hr, 25 micrograms/hr, 50 micrograms/hr, 75 micrograms/hr and 100 micrograms/hr. *N.B.* patches require changing every 72 hours.

When the first patch is applied it will take 12-18 hours before maximal analgesia is achieved. The starting dose should be at an appropriate conversion from the current opioid in use [refer to page 41 Opioid Conversion Table]. The patch strength should not be increased until it is due to be changed, but an immediate-release opioid should always be prescribed for breakthrough pain.

Also, once a patch is removed, there will continue to be some absorption of fentanyl from the skin for a further 12-18 hours.

Buprenorphine Patches

Buprenorphine is available in a number of formulations which vary in duration of activity. **Butrans** patches are changed weekly and **Transtec** patches twice weekly. As with fentanyl there is a delay in onset of analgesic effect of 18-24 hours after first application of a patch, and a similar delay for the effect to wear off after patch removal. An immediate-release opioid should be prescribed for breakthrough pain (see conversion table or access the online "Pallicalc" at http://book.pallcare.info/index.php for appropriate doses).

Common side-effects of opioids

Constipation

Virtually all patients become constipated on regular opioids. Prescribe a regular laxative to prevent constipation. Increase the dose as the opioid dose increases [refer to page 12].

Nausea

May occur when starting or increasing opioids, therefore prescribe an anti-emetic for use if necessary [refer to page 13].

Dry Mouth

This is a common side effect. Local measures can be very helpful *e.g.* ice cubes, pineapple chunks as well as artificial saliva (*e.g*. AS Saliva orthana spray or Oralbalance gel). Check for oral candidiasis and treat appropriately

Drowsiness

May occur when opioids are started or the dose is increased, but it is usually transient and will reduce over a few days.

Opioid toxicity

Life threatening opioid toxicity due to respiratory depression is rare if opioids are titrated safely and according to agreed guidance. Naloxone should only be used to reverse opioid toxicity if respiratory depression is present [refer to page 39].

Features of non-life threatening opioid toxicity include

- Sedation
- Hallucinations
- Confusion
- Myoclonus

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

Management of suspected toxicity includes:

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

N.B. When sedation is required (to address problems of anxiety, restlessness or agitation) it should not be achieved by increasing the opioid dose, instead a more appropriate sedative medication should be prescribed.

Specific pain syndromes

It is helpful to identify the following syndromes which benefit from particular management strategies:

Metastatic bone pain

- Paracetamol
- NSAIDs
- Palliative radiotherapy – refer to oncology team
- Bisphosphonates *e.g.* pamidronate or zoledronate infusion (check renal function and dental status before treatment)

Back pain and malignant spinal cord compression in cancer

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

- Commence dexamethasone 8mg bd immediately
- Urgent discussion with oncology.
- Arrange urgent MRI of entire spine

Headache from raised intracranial pressure in cancer

May present in primary cerebral tumour or cerebral metastases.

- Give dexamethasone, starting at 8 mg bd in the morning and at lunchtime. May cause insomnia if given later in the day.
- If there is no response within 7 days discontinue the dexamethasone.
- If patient responds, gradually reduce the dosage to a maintenance dose.
- Consider palliative radiotherapy – refer to oncology team

Bowel colic

- Assess for and manage constipation.
- Consider anti-spasmodic. Hyoscine hydrobromide (Kwells) 300 micrograms SL tds or hyoscine butylbromide (Buscopan) 10mg - 20mg PO/SC PRN.

- In bowel obstruction, the oral route is not appropriate for drug administration (see section on intestinal obstruction).

Liver capsule pain

- Dexamethasone 4mg - 8 mg od or NSAID +/- opioids.

Neuropathic pain

- Analgesic ladder (see earlier) – pain may be opioid responsive.
- Adjuvant analgesics:
    - Dexamethasone: 8mg od to relieve nerve compression
    - Amitriptyline: Starting dose 10mg - 25mg at night and titrate upwards
    - Gabapentin: Starting dose is 300mg od (elderly patients 100mg); titrate upwards as tolerated.

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

Interventional procedures for pain

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

TENS (Transcutaneous Electrical Nerve Stimulation)

For localised neuropathic pain. Consult a physiotherapist.

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 (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.
- 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.
- 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 rectally, or by CSCI. Diclofenac should not be combined with any other drugs in the syringe driver and should be diluted with 0.9% sodium chloride with a minimum volume of 20 mls within the syringe.

Transdermal opioids and CSCI

If setting up a CSCI via a syringe driver in a patient using transdermal patches, **continue with the patch** at the appropriate interval 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 page 41 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 - 5mg
Levomepromazine	5mg – 12.5mg
Cyclizine	150mg
Metoclopramide	30mg - 60 mg

Respiratory secretions and bowel colic

Drug	Usual starting dose range/24hours
Glycopyrronium bromide	600 micrograms – 2.0 mg
Hyoscine butylbromide (Buscopan)	40mg - 120mg

Terminal agitation and restlessness

N.B. exclude urinary retention and pain [refer to page 24].

Drug	Usual dose range/24hours	Comments
Midazolam	10mg - 60mg Add in levomepromazine if agitation not controlled with 60mg	Useful if anxiety is a feature.
Levomepromazine	25mg - 50mg	Useful if psychotic features are present.

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 20mg over 24hours and increasing as required.

Pre-emptive prescribing of midazolam 5-10mg SC or IM as PRN dose to be given if a seizure occurs. If uncontrolled seizures despite higher doses (>60mg midazolam) 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)
- Exclusion of malignant bowel obstruction

Treatment

- Correct **reversible causes**
- 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

- Senna 7.5 – 15mg usually at night and increasing as necessary
  Side effects: can cause cramps and should be avoided in bowel obstruction

- Combination laxatives: 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.

- Osmotic laxatives *e.g.* Macrogols [Laxido]).
  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

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 such as opioids, tricyclic antidepressants, phenothiazines, hyoscine
- Gastrointestinal obstruction [refer to page 15].

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
- Treat any reversible causes *e.g.* hypercalcaemia
- Prescribe a regular oral anti-emetic.
- 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.

First line medication

- Haloperidol 1.5 mg-3 mg as a single night time dose (***N.B.*** potential risk of arrhythmias)
- Cyclizine 50 mg tds (often combined with haloperidol)
- Levomepromazine 5-12.5mg as a single night time dose
- Metoclopramide 10 mg-20 mg tds especially if improved gastric emptying is required

Possible adjuvant medication

- Lorazepam 500 micrograms sublingual or PO PRN may be helpful where anxiety is a precipitating factor
- Dexamethasone 4mg - 16 mg/day for raised intracranial pressure.
- Proton pump inhibitors *e.g.* lansoprazole 30mg for gastric irritation.

N.B. Theoretically the prokinetic effect of metoclopramide will be lost if prescribed with an antimuscarinic drug such as tricyclic antidepressants, cyclizine or levomepromazine.

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

Management of gastrointestinal (GI) obstruction in palliative care

Symptoms/Signs indicating Malignant Bowel Obstruction (MB0)

-Known or suspected intra-abdominal malignancy
-AXR or CT scan unless clinical condition make this inappropriate in the face of clear clinical diagnosis
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

Management plan

- Constipation excluded by digital rectal exam or radiology
- Baseline bloods to assess current status (if appropriate):
    - FBC
    - Biochemistry
    - 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 chemosensitive disease.
- Referral to Specialist Palliative Care Team
- Consider IVI if fluid depleted or significant thirst
- Consider NGT only if surgery 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 contra-indications):

- Metoclopramide 30-60 mg/24 hours via CSCI (syringe driver)
- Trial of dexamethasone 6.6 – 13.2mg IV or SC mane with PPI cover
- Docusate 200mg BD
- Opioid at appropriate dose for tumour pain

PRN medication:

- Metoclopramide for nausea 10- 20mg SC / IV PRN
- Opioid at appropriate breakthrough dose for tumour pain (usually one-sixth of total daily dose of morphine or oxycodone) to use prn
- Hyoscine butylbromide 10-20mg SC hourly with maximum of 60mg / 24 hours in case colic develops.

If colic develops switch to regimen below:

For patients with colic

- Hyoscine butylbromide 60mg - 120mg / 24 hours as an antisecretory agent and antispasmodic
- Levomepromazine 5mg – 12.5 mg / 24 hours as an antiemetic
  (Both via CSCI (syringe driver))
- Trial of dexamethasone 6.6 – 13.2mg IV or SC mane with PPI cover
- Docusate 200mg BD
- Opioid at appropriate dose for tumour pain

PRN medication

- Buscopan 10-20mg SC hourly with maximum of 60mg / 24 hours for colic
- Opioid at appropriate breakthrough dose for tumour pain
- Levomepromazine 5mg SC 6 hourly PRN for nausea

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. Need to think ahead in these groups of patients.

Whilst offering immediate treatment consider **reversible causes**: recent drug changes, organ failure, hypoxia, infection, hypercalcaemia, dehydration, encephalopathy, hypo/hyperglycaemia.

Management

- Offer a calm, well-lit environment, careful explanations, consistent carers and ideally presence of a close relative
- Explain and discuss with family/carers the treatment proposed
- In absence of abnormal behaviour or perception or psychosis:
    - Reduce anxiety if necessary with lorazepam 500 micrograms - 1mg SL or PO or midazolam 2.5mg - 10mg SC PRN initially
- In the presence of abnormal behaviour or perception or psychosis:
    - If wishing to avoid excessive sedation give haloperidol 1mg - 5mg SC or 2mg -10mg orally (note subcutaneous : oral potency haloperidol 2:1)
    - Should sedation be required, use levomepromazine 12.5mg - 50mg / 24 hrs in CSCI via syringe driver or orally. If risk of seizures, combine with midazolam SC [refer to page 40].
- Decisions about the starting doses are based on expected length of life, degree of agitation and distress
- Acute confusion is 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). Often there is a humoral component irrespective of the presence 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] x0.02} + 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 (pamidronate, zoledronic acid 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

The uncomfortable awareness of breathing is a frightening symptom, and management of that fear and anxiety is essential. Episodes of hyperventilation or panic are a common feature.

Assessment

This includes history, examination and appropriate investigations. Reversible causes should be treated when 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.

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 breathless patients
- Exploration of fears, concerns and previous experiences
- Explanation and reassurance: *e.g.* "an awareness of breathlessness is normal after exercise and is not dangerous"
- Cool draught or hand held fan, loosen tight clothes
- Simple advice: drop shoulders, breathe all the way out.
- 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 referral to a specialist palliative care team and physiotherapist. *E.g.* Refer to Pilgrims Hospices' breathlessness management service.

Pharmacological treatment

Opioids

- Aim to reduce the sensation of breathlessness (supported by systematic review findings)
- Improvements are seen at doses that do not cause respiratory depression
- Starting dose: morphine 2mg - 5 mg PO 4 hourly prn (lower dose in respiratory failure).
- If more than 2 doses are needed within a 24 hr period, prescribe a morphine long acting preparation (*e.g.* Zomorph) regularly and titrate the dose according to response.
- In patients already taking regular opioids for pain then increase regular dose by 25-30%
- The appropriate 4 hourly "breakthrough" 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.
- *E.g.* lorazepam 500 micrograms-1mg PRN/QDS or oxazepam 5-10mg PRN/QDS

Nebulised 0.9% sodium chloride

- Helpful for sticky bronchial secretions that are difficult to expectorate.

Oxygen

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

Parenteral medication

If the patient is unable to take oral medication, then morphine or equivalents at the appropriate conversion dose and midazolam can be given by CSCI and PRN (see section on end of life care).

The dying patient

Recognising the dying patient

- The multi-professional team may agree that the patient is dying
- The following criteria may 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

- **Communicate** to everyone involved to confirm the current situation. Clarify patient/family expectations, as well as that of the professionals involved:
  - Explain the ceiling of treatment rationale and clearly document.
  - DNACPR form should be completed and similarly discussed.

- **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.

- **Ensure** the symptoms are controlled and appropriate PRN Medications prescribed

  Appropriate PRN SC medications are:
  - Analgesia *e.g.* morphine 2.5 – 5mg 2 hourly if on no regular analgesia or at the appropriate dose if they are already on opioids.
  - Anti-emetic: *e.g.* haloperidol 1.5mg - 3mg 6 hourly or cyclizine 50mg 8 hourly or levomepromazine 5mg -12.5mg prn 6 hourly
  - Sedative: midazolam 2.5mg - 10mg prn 2 hourly
  - Antimuscarinic for respiratory secretions: glycopyrronium 200 – 400 micrograms 2 hourly or hyoscine butylbromide 20mg 2 hourly

- In the community there is a need for anticipatory prescribing of these medications including the 0.9% saline or water for injections.

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

- CSCI prescriptions should include an appropriate range 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).

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

- **Assess** patient's religious or spiritual needs.

- **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).

For advice out of hours please ring
Pilgrims Hospices 01233 504133 – 24 hour line for East Kent locality patients

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.

General interventions

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

Drug treatment

Treatment should be commenced as soon as symptoms become apparent:

- Glycopyrronium is the preferred drug because:
    - No central side effects
    - Potent and efficacious
    - Longer half-life than other antimuscarinics
    - Dose: 200 micrograms – 400 micrograms SC PRN and 600 micrograms to 2mg / 24 hours by CSCI.

Other medications that can be used are

- Hyoscine butylbromide: 20 mg SC PRN and 40mg - 120mg over 24 hours by CSCI.
- Hyoscine hydrobromide: 400 micrograms SC PRN and 1.2mg – 2.4mg over 24 hours by CSCI. *N.B.* Can cause sedation or agitation

Other Measures

- 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 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 treatment

Drug management of restlessness at the end of life

Aim of treatment should be 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 specialist palliative care advice.

Midazolam

- 2.5mg - 10mg SC stat and PRN 4 hourly
- Consider midazolam 10mg - 60mg per 24 hours by CSCI. This can be gradually increased according to its response

Levomepromazine

- Often useful in situations which fail to respond adequately to midazolam and maybe used in addition to it
- 12.5mg – 25mg SC PRN
- 25mg - 100mg / 24 hours via CSCI if ongoing sedation required

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

Symptom control 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 [refer to page 27]
- Neuropathic agents can cause arrhythmias (tricyclic antidepressants) or fluid retention (pregabalin and gabapentin)

Nausea and vomiting

- Consider toxicity from medication especially digoxin.
- Domperidone is first choice.
- Cyclizine may worsen severe heart failure
- Haloperidol, levomepromazine and metoclopramide may predispose to rhythm problems. If low blood pressure is a concern haloperidol and levomepromazine may exacerbate this. Use lowest dose possible.
- Potential risks have to be balanced against good symptom control in end of life care.

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 19.

Cough

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

Constipation

- Avoid ispaghula husk because of fluid requirements
- If using macrogols, Idrolax is preferred rather than Movicol due to its lower sodium content

Miscellaneous

- When using antidepressants – avoid tricyclic antidepressants and venlafaxine where 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 regimes
- 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.

Symptom management in end stage renal disease

Pain

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

The WHO ladder is still applicable.

- Step 1- Paracetamol can be used safely unless severe renal impairment (EGFR <10) when dose reduction is required *e.g.* 500mg QDS.
- Step 2 - Tramadol is often used in reduced dose (*e.g.* 50mg BD if eGFR <20).
- Step 3 - General advice with opioids is to dose reduce and increase 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 IR oxycodone may be preferable to IR morphine.

Buprenorphine, fentanyl and alfentanil are the opioids least likely to accumulate. Refer to page 41 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 need dose adjustment in renal impairment (see BNF) If the patient is on dialysis specialist advice may be required.

Nausea and vomiting

All anti-emetics can accumulate in renal impairment. The choice of anti-emetic will depend on the cause of nausea and vomiting. Monitor for side effects.
Examples of anti-emetics and doses which can be used are:

- Domperidone 10mg PO QDS.
- Haloperidol 500 micrograms – 1.5mg PO/SC PRN or 1.5mg - 3mg via CSCI over 24hrs
- Cyclizine 50mg tds PO/SC or 150mg via CSCI over 24 hours.

Dyspnoea

General management is the same.
Opioids may provide effective symptom relief.
The same precautions apply as per the use of opioids with pain (above).
Benzodiazepines accumulate in renal impairment but can be used in the same manner as in the breathlessness section [refer to page 19]

Respiratory tract secretions

There is no difference in the management in renal failure [refer to page 23].

Restlessness 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 5-10mg over 24hours
This can be gradually titrated up according to severity of anxiety or agitation.

Itching

This can be challenging to manage.
Topical emollients are first line treatment.
Chlorpheniramine 4mg tds/qds or promethiazine 25mg bd or 10mg - 20mg tds can be tried.
Gabapentin 100mg daily and pregabalin 25mg daily has recently been proven to be successful in the treatment of pruritus
Discuss with Palliative Care Team regarding other options if these measures are not successful.

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 sugar in the range of 7-17 mmol/L.
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

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.

General management

- Dietary advice - a low carbohydrate diet is not always appropriate in patients approaching the end of life.
- Reassess medication in particular the corticosteroid dose and reduce if possible.
- Exclude other reversible causes such as infection
- Keep monitoring blood sugar levels tests 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.
- 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.

Management of new or of type 2 diabetics approaching the end of life

- Cachectic patients are likely to have a poor response to oral hypoglycaemic agents so consider insulin therapy early.
- Avoid metformin in patients with advanced cancer.

Blood Sugar	Management
11 - 17 mmol/L	Start gliclazide 40mg and titrate according to response to 160mg BD.
17 - 27 mmol/L	Start gliclazide 80mg OD and titrate according to response to 160mg BD. If control still not achieved then consider adding long acting Insulin 10 units nocté.
If 17 - 27 mmol/L and moderate or severe ketonuria present	Add long acting Insulin 10 units nocté. If symptomatic then consider use of short acting soluble insulin 4-6 units to reduce sugar <17 mmol/L.
>27 mmol/L	Consider transfer to the acute sector for more intensive management if appropriate. Short acting soluble insulin 4-6 units can be used to reduce the blood sugar <17 mmol/L.

- When vomiting or not able to eat then oral hypoglycaemic agents will need to be dose reduced by 50%. These will need to be stopped altogether in the terminal phase.
- In type 2 diabetics on insulin, insulin is needed even when unable to eat to prevent developing a hyperosmolar non-ketotic state although a 25% dose reduction should be considered. Insulin should also be stopped in the terminal phase.

Management of type 1 diabetics approaching the end of life

- The appropriate management of these patients does depend on their prognosis.
- In type 1 diabetics, insulin is always needed to prevent developing ketoacidosis which would be fatal if untreated. Stopping insulin altogether in these patients, therefore, should only be considered in the last days of life.

Oral Intake	Management
Eating fairly normally	No change in previous management of patient's diabetes.
Decreased appetite	Monitor blood sugar on a daily basis and reduce insulin prescription step by step until blood sugar stable.

Severe anorexia or vomiting	Convert to long acting insulin 10 units nocté or 25% of previous total daily dose if on higher doses. Blood sugar will need to be monitored regularly Consider admission to the acute sector if appropriate after discussion with palliative care team

- Long acting insulin is the most effective approach, particularly as the condition of the patient deteriorates. Alternatively short acting soluble insulin can be given after meals in order to prevent the hypoglycaemia that might result if meals aren't finished whilst on a longer acting insulin.

Management of hypoglycaemia

- This is a significant risk as anorexia develops.
- Glucagon may not be effective, especially in the presence of liver metastasis.
- 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, fizzy drinks, cordials or glucose/dextrose tablets and similar gels are available for buccal use. PEG tubes can be used as a route of administration for fizzy drinks or undiluted cordial if required.
Unconscious	Place the patient in the recovery position as this is the priority if unconscious. The oral route should not be used but the buccal route is helpful 1mg Glucagon can be given intramuscularly if available. If unavailable or ineffective then intravenous access and a 50-100ml bolus of 20% Dextrose given if appropriate. Consider transfer to the acute sector if in line with the patient's ceiling of appropriate management.

- Repeat observation and blood sugar monitoring regularly until blood sugar is stable at over 4 mmol/L.
- Give foods rich in carbohydrate that release their energy slowly to reduce the risk of recurrence.
- Review insulin or oral hypoglycaemic agents to minimise risk of recurrence.

Symptom management in end stage neurological disease

The pathway for care in end stage neurological conditions has been developed and is available at http://www.ncpc.org.uk/neurological-conditions. Liaison with specialist teams already involved with patients is key to successful management of these situations.

Symptom management in end stage Parkinsonism

Usual Treatment

The NICE clinical guideline on Parkinson's disease (http://www.nice.org.uk/CG035) 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.

Drugs used for symptom relief

Standard symptom control regimes 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, metoclopromide) 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 key and requires competent communication skills
- Communication needs to be open between patients, families and all professionals involved
- Listen to understand and not just to hear
- The non-verbal message you give is more important than the verbal one

Breaking bad news

The following steps may help in structuring these conversations:

1. Preparation: Setting, who should be present and up-to-date information
2. Find out what the patient knows already: How close are the patient's ideas to the actual situation? Can you use their words and phrases?
3. Find out what the patient wants to know and adjust your information accordingly
4. Give a warning shot and allow time
5. Allow the patient to refuse information at this time: Rather than denial this can be part of a healthy adjustment
6. Explain if requested: Honest and simple explanations in small chunks Avoid jargon and check understanding. Encourage questions.
7. Elicit concerns and encourage ventilation of feelings and emotions: Therapeutic in itself. Correct immediate misunderstandings. Identify appropriate longer term support.
8. Summary and plan: Confirm understanding for both parties. Agree timetabled future plan
9. Offer realistic availability and support: Early follow-up mechanism for further contact with professionals in the meantime
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
Patient involvement in the discussions is important. If the patient is not to be involved in discussions you must be clear that the patient does not wish to discuss or that there is a risk of significant psychological harm.
When the patient is imminently dying the discussion should focus on the imminent death of the patient rather than the CPR decision which is secondary. The family's role is to inform the process 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 ever ask “Shall we resuscitate your relative?”

Use the same steps as when breaking bad news during CPR discussions

1. Preparation.
2. Seek permission to explore future course 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 going?”
4. Explain to patients and their families that attempts at CPR are very unlikely to be a successful for the significant majority of patients in the palliative phase of their illness. Remember to chunk and check 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 well as we can there are some procedures that will not help and will probably cause you more suffering; such as CPR / ventilation / artificial nutrition, *etc*”
5. Include other ceilings of treatment that are appropriate and future care wishes such as preferred place of 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

This is meant only as a guide as to how a discussion may be lead. The exact phrases used should be determined by the patient and their responses to previous questions or information.

Use electronic Palliative Care coordination systems such as *Share My Care* to communicate across specialties and disciplines.

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 a second opinion could be sought

Further reading

"Decisions relating to cardiopulmonary resuscitation", a 2007 joint statement from the British Medical Association, the Resuscitation Council (UK) and the Royal College of Resuscitation

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.

Your own needs

- All of us will have to break bad news to a patient, a relative or a carer or have other difficult discussions. It is important to consider how best you can develop your skills
- Communication skills training, and in particular training with the use of actors to offer feedback in a "safe" setting, can form a very valuable training tool for all those involved with communication near the end of life but in particular when delivering bad news.

Adult specialist palliative care units and teams in Kent

Ashford

Pilgrims Hospices in Ashford
Tel: 01233 504133 (24 hour)
Fax: 01233 504132
Email: PH.Pilgrims-Ashford@nhs.net

William Harvey Hospital Macmillan Palliative Care Team
Tel: 01233 633331 x88352
Fax: 01233 616867

Canterbury

Pilgrims Hospices in Canterbury
Tel: 01233 504133 (24 hour)
Fax: 01227 812606
Email: PH.Pilgrims-Canterbury@nhs.net

Kent and Canterbury Hospital Palliative Care Team
Tel: 01227 766877 Bl 238 or Bl 007

Dartford, Gravesham and Swanley

EllenorLions Hospice (In-patients and day therapy)
Tel: 01474 320007
Fax: 01474 534633

EllenorLions Hospice (Hospice at Home Team)
Tel: 01474 538508
Fax: 01474 326260

Darent Valley Hospital Palliative Care Team
Tel: 01322 428293
Fax: 01322 428294

Hastings

St Michael's Hospice
Tel: 01424 445177
Fax: 01424 721255

Conquest Hospital Macmillan Palliative Care Team
Tel: 01424 758016

Maidstone

The Heart of Kent Hospice
Tel: 01622 792200
Fax: 01622 718920

Maidstone Hospital Macmillan Palliative Care Nurse
Tel: 01622 225024
Fax: 01622 225116

Margate

Pilgrims Hospices in Thanet
Tel: 01233 504133 (24 hour)
Fax: 01843 233931
Email: PH.Pilgrims-Thanet@nhs.net

QEQM Hospital Palliative Care Team
Tel: 01843 225544 x65153 x65074
Fax: 01843 234529

Medway and Swale

Wisdom Hospice
Tel: 01634 830456
Fax: 01634 845890

Medway Maritime Hospital Palliative Care Team
Tel: 01634 833807
Fax: 01634 833807

Tunbridge Wells

Hospice in the Weald
Tel: 01892 820500
Fax: 01892 820520

Kent and Sussex Hospital Macmillan Palliative Care Team
Tel: 01892 632346
Fax: 01892 632939

Further Reading

www.palliativedrugs.com
Palliative Care Formulary 5th Edition available from palliativedrugs.com
More detailed palliative care guidance and access to “pallicalc” and “palliap”:
http://book.pallcare.info/index.php

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.

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 10mls with 0.9% sodium chloride
3. If intravenous access is available go to step 4; otherwise administer 40 micrograms intramuscularly.
4. Administer 0.5ml (twenty micrograms) intravenously (**see notes in bold above**) every two minutes until the respiratory rate is satisfactory.

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

	Midazolam	Metoclopramide	Levomepromazine	Hyoscine Hydrobromide	Haloperidol	Glycopyrronium Bromide	Diamorphine & Morphine	Cyclizine
Hyoscine Butylbromide	✓	Not Applicable	✓	Not Applicable	✓	Not Applicable	✓	⊘
Cyclizine	✓	⊘	Not Applicable	✓	✓	✓	✓	
Diamorphine	✓	✓	✓	✓	✓	✓		
Glycopyrronium Bromide	✓	Not Applicable	✓	Not Applicable	✓			
Haloperidol	✓	Not Applicable	Not Applicable	✓				
Hyoscine Hydrobromide	✓	Not Applicable	✓					
Levomepromazine	✓	Not Applicable						
Metoclopramide	✓							

Key

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

Opioid Conversion Table

Dosage conversion between opioids

Morphine				
ORAL			Parenteral	
24 Hour total morphine		Morphine modified release tabs/caps	Morphine oral solution or tabs*	Morphine by CSCI	Morphine prn SC*
mg/24 hrs		mg/12 hrs	mg/4 hrs	mg/24 hrs	mg/prn
30		15 BD	5	15	2.5
60		30 BD	10	30	5
100		50 BD	15	50	7.5
120		60 BD	20	60	10
180		90 BD	30	90	15
240		120 BD	40	120	20
360		180 BD	60	180	30
480		240 BD	80	240	40
600		300 BD	100	300	50
800		400 BD	130	400	

Morphine	Oxycodone			
ORAL	Oral		Parenteral	
24 Hour total morphine	Oxycontin modified release tabs	Oxynorm oral*	Oxynorm by CSCI	Oxynorm prn SC*
mg/24 hrs	mg/12 hrs	mg/4 hrs	mg/24 hrs	mg/prn
30	10 BD	2.5	10	2.5
60	15 BD	5	15	2.5
100	25 BD	10	25	5
120	30 BD	10	30	5
180	45 BD	15	45	7.5
240	60 BD	20	60	10
360	90 BD	30	90	15
480	120 BD	40	120	20
600	150 BD	50	150	
800	200 BD	70	200	

Morphine	Diamorphine		Alfentanil
ORAL	Parenteral		Parenteral
24 Hour total morphine	Diamorphine by CSCI	Diamorphine prn*	Alfentanil by CSCI
mg/24 hrs	mg/24 hrs	mg / prn	mg/24hours
30	10	2.5	1
60	20	5	2
100	30	5	3
120	40	7.5	4
180	60	10	6
240	80	15	8
360	120	20	12
480	160	25	16
600	200	35	20
800	250	40	25

Morphine	Fentanyl**	Buprenorphine**	
ORAL	Transdermal	Transdermal	
24 Hour total morphine	micrograms/hr	micrograms/hr	
mg/24 hrs		Butrans	Transtec
30	12	10	
60	25	20	
100	37		35
120	50		52.5
180	75		70
240	100		105
360	150		140
480	200		
600	Please		
800	ask advice		

Other opioids

From total daily opioid dose (mg)	To get to the equivalent 24 hour total oral morphine (mg)	
Codeine	x	0.1
Dihydrocodeine	x	0.1
Hydromorphone	x	5
Oxycodone (oral)	x	2.0
Tramadol	x	0.1
Diamorphine (parenteral)	x	3

Higher doses of oxynorm and morphine are too large a volume for SC injection.

*** PRN doses are the recommended breakthrough doses for those patients on the specified 24hour doisng of the strong opiate**

****Conversions to and from Fentanyl and Buprenorphine patches should be checked against manufacturer's guidance.**
Consider reducing opioid doses by 25% when switching to allow for incomplete cross-tolerance

N.B. The conversions given in this table are approximate and may need to be adjusted according to response
Advice from the palliative care teams should be sought at higher dose conversions

Alternatively www.book.pallcare.info/index.php
palliacalc: http://book.pallcare.info/index
The conversions given in this table are a pragmatic mix of the "traditional" and "progressive" methods used in the on-line converter tool. Dose conversions should be individualised. They are likely to need to be adjusted according to response. Consider a dose reduction of 25-50% to allow for incomplete cross-tolerance.